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BRAIN.

PART I., 1900.

Original Articles and Clinical Cases.

ON THE EXCITABILITY OF NERVOUS MATTER, WITH ESPECIAL REFERENCE TO THE RETINA.[1]

BY AUGUSTUS D. WALLER, M.D., F.R.S.

I HAVE not failed to pass through the preparatory searchings of mind incidental to the delivery of a presidential address, nor to sacrifice to custom by the deliberate writing of a bulky manuscript heavily charged with midnight reflections. But one outcome of those reflections has been an intimate conviction that such deliberate writing is fitted only for the deliberate reading of the fireside, and that it would be impossible for me, within reasonable limits of time, to make my meaning fully clear, by reason of the detail in which it has become enveloped. I have therefore thought preferable to cut myself adrift from the manifold detail of written thought, and endeavour, however lamely and ungrammatically, to at least indicate to you what are the chief new facts that I am selecting to lay before you, and what is the vein of sense which to my mind renders them of neurological value.

---

[1] Presidential Address to the Neurological Society, February 8, 1900.

My contribution to our common theme is coloured from the laboratory—which, however, will not be accounted to me for unrighteousness in a Society whose distinguishing characteristic it is that it forms a meeting place of complementary interests—from the domain of the laboratory as well as from the hospital—the two chief colours, so to speak, that together make for the neurologist the white light of his knowledge. Nor—to continue the analogy—shall I be unmindful of a third colour by which the triangle of interests is completed in our Society, and I shall try to indicate in the course of my address points of contact with psychological doctrine, of some of the dry facts that belong in first place to physiological analysis.

Let me briefly summarise the subject-matter that I hope to review this evening. I divide it into three chapters, and shall hope under each of these three heads to clearly develop and fix at least one idea of elementary neurological interest.

In Chapter I. I shall briefly refer to a method of procedure, and insist upon the principle that systematic observation of the electrical signs of life yields valuable information.

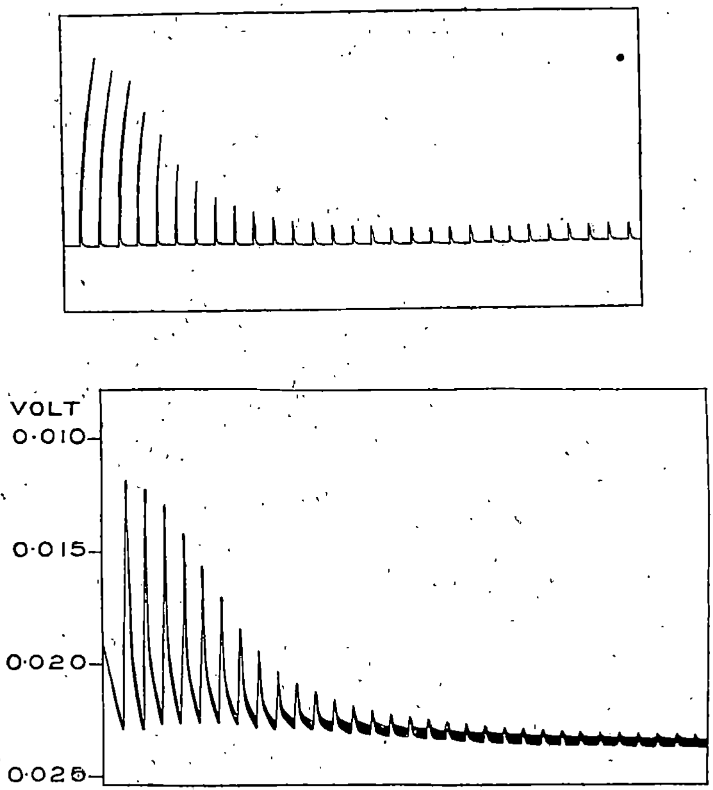
In Chapter II. I shall consider at some length the constructive and disruptive phenomena of which nervous matter is the seat. I shall do this with particular reference to electrical changes produced in the retina by light. I shall briefly describe those changes, and derive from them the conclusion that light excites in the retina a double process of simultaneous decomposition and recomposition; and in conclusion to this chapter I shall take occasion to describe the specific action of protoveratrine upon medullated nerve, viz., an abolition of the positive reaction after action. Incidentally to this matter I shall also refer to the great exhaustibility of non-medullated nerve, and to the slight exhaustibility of the retina as compared with the apparent inexhaustibility of medullated nerve-fibres.

Chapter III. will consist in the consideration of what I term the "law of response," in so far as it can be ascertained by study of the quantitative relations between physical exciting cause and physiological excited effect. My special conclusion *qua* the retina will be:—that the cause-effect curve is an S-shaped or sigmoid curve. My general argument will be:—that a sigmoid curve expresses the ratio between physical stimulus and physiological effect, as well as between physical stimulus and psychological effect.

I.—The Electrical Sign of Life.

Living nervous matter—all living matter indeed—is "excitable" and responds to its "call-from-without" by some form of movement—chemical movement, mechanical movement, electrical movement. An animal gives sign of life by moving. An isolated muscle gives sign of life by contracting when stimulated, and we are able by more or less refined methods to show that such contraction is accompanied by physico-chemical changes—production of acid, evolution of carbon dioxide, rise of temperature, electromotive action. An ordinary nerve, normally connected with its terminal organs, gives sign of life by means of muscle, which by direct or reflex path is set in motion when the nerve-trunk is stimulated. But such nerve separated from its natural termini, isolated from the rest of the organism, gives no sign of life when excited, either in the shape of chemical or of thermic changes, and it is only by means of an electrical change that we can ascertain whether or no it is alive. The eye—the retina—is known to us as a living organ in our own persons when we see an external object. By various devices of the laboratory we measure quantities of stimulant light and differences of excited sensation. The isolated organ—an entire eyeball, or its isolated retina—is best known to be alive or not by means of its electrical response or silence when it is put to the question by its natural stimulus light.

In the three cases named the most general and most delicate sign of life is then the electrical response, and I shall hope to show that the electrical signs of life studied



FIGS. 1 AND 2.

Simultaneous record of a series of muscular contractions and of the corresponding electrical responses.

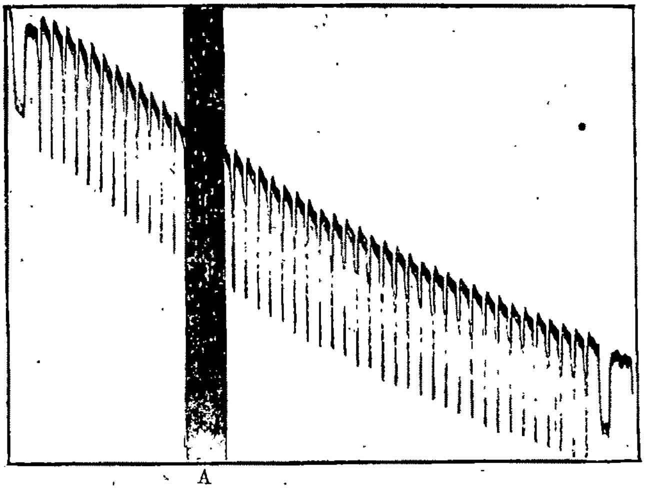
The muscle (frog's gastrocnemius) connected to an isometric myograph (record A), and led off to a galvanograph (record B), is excited by tetanisation of the sciatic nerve at one minute intervals. Each period of tetanisation lasts six seconds.

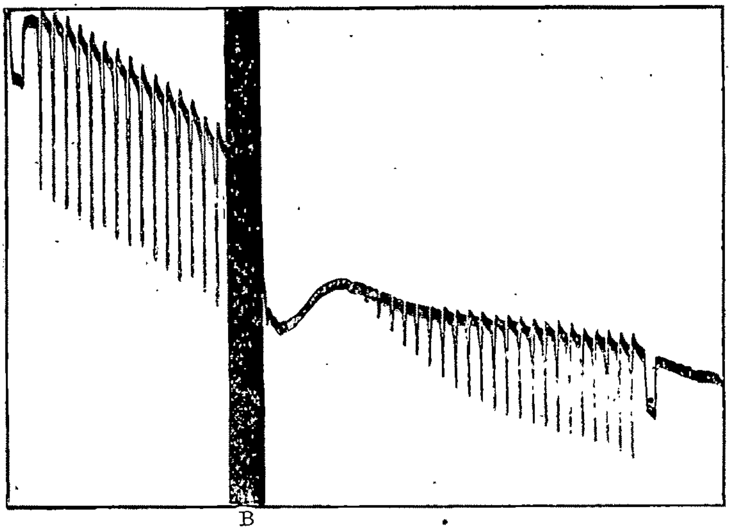
and measured in the laboratory upon these three organs afford very definite contribution to fundamental principles of neurology.

I do not now propose to dwell upon either nerve or muscle. Let me, however—towards establishing in your judgment the general credit of the electrical sign of life—make very brief allusion to experiments upon these two tissues.

To muscle I shall appeal solely to make good the preliminary position. Compare, *e.g.*, these two simultaneous records—(*a*) of muscular contractions, (*b*) of the electrical responses belonging to the contractions. The electrical effects are to all intents and purposes a replica of the contractions; and if you admit contraction to be valid physiological testimony, you must admit the electrical response to be at least equally valid. The parallelism—as regards fatigue of the end-plate in this case—between the two kinds of record is close, not indeed quite perfect; but of the two versions I should say that the galvanometer gives a rather more faithful report than does the myograph as regards the quantity of chemical change underlying the visible mechanical change.

In the case of nerve, which has no mechanical expression of itself otherwise than by means of muscle, we may, and indeed must, rely upon the galvanometer alone for information as to its physiological state. And nerve—the most hopeless tissue to investigate by way of the indications of muscle, hopeless because nerve is so tough and its terminals are so tender—is an almost ideal sample of living matter upon which to test the comparative effects of all manner of reagents, when the galvanometer is made to be its organ of expression. For we have in our hands a living tissue, absolutely isolated from all other tissues, responding with unfailing regularity so long as nothing more is done to it, and therefore informing us whether or no any given experimental modification affects it. I will content myself by exhibiting to you two typical nerve-records illustrating what I have already on previous occasions at the Society claimed as the distinctive excellence of the method, viz., the clearness of its results. Figs. 3 and 4 are the records of two experiments in which the effects of two gases are tested upon an isolated nerve, their incidence being signalled by the vertical dark bar. There is no doubtful or obscure result. The gas A had no action. The gas B had an evident action.





FIGS. 3 AND 4.

Two records of series of electrical responses of nerve, upon which effects of gases are tested. Excitation by tetanisation for 7·5 secs. at one minute intervals. The time during which the nerve is submitted to the influence of the gas is signalled by a vertical dark bar across the record. Gas A is an indifferent gas. Gas B is an anæsthetic gas.

N.B.—The scale in these and other records gives the approximate voltage of deflections.

II.—CONSTRUCTIVE AND DISRUPTIVE MOVEMENT.

Let us take as a point of departure "the axiom of general physiology," to which we all subscribe.

Living nervous matter—all living matter—is the seat of two opposite tendencies, integrative and disintegrative, synthetic and analytic, centripetal and centrifugal, constructive and disruptive, anabolic and katabolic, positive and negative. Each act of life is act of death. A muscle by the act of contraction, a nerve-cell by the act of explosion, manifests energy, expends stored matter, undergoes fatigue, and requires to be replenished by the converse act of nutrition. Living tissue, inasmuch as it *is* living, is also dying tissue, ceaselessly evolving energy, ceaselessly "re-storing" energy.

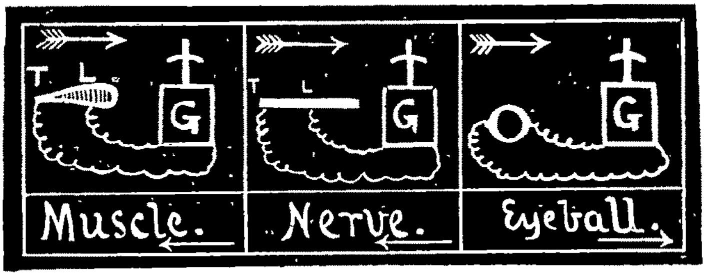


FIG. 5.

To show direction of currents in muscle, nerve, and eyeball. Arrows at top of figure indicate direction of normal current ("current of injury"). Arrows below indicate direction of electrical response to excitation ("current of action").

The double chemical current of which living matter is the centre, manifests itself by actual chemical and structural consequences when it has been sufficiently intense or sufficiently prolonged. Its weakest and briefest pulsations are manifested by electrical changes.

Taking as our line of departure, or zero level, the low-grade continuous chemical change normal in the unexcited state of living tissue—muscle, for example—we have a greater electro-motive action with greater activity of muscle, a lesser electro-motive action with lesser activity. There is no difference of chemical and electrical state between any two points of an ideally normal uniform muscle—all points are equally alive. If one of the two points be positively active, it will be positively electro-motive. If one of the points be negatively active, it will be negatively electro-motive.

Living muscle—or living nervous matter—or, indeed, any living matter—is excitable, and the most delicate physical sign of that excitability is electromobility, viz., the capacity of manifesting an electrical change in response to excitation. Such electrical change in response to excitation may be positive or negative, positive with augmented disintegration, negative with augmented reintegration.

A muscle, a nerve, an eyeball connected with a galvanometer, as shown in these three sketches, manifests current which we may designate as being upwards (in the tissue) or to the right (through the galvanometer), or positive.

This upward current is due in each case to electro-motive action at the point of injury, and gradually subsides—most rapidly in the case of the eyeball, which is apt to exhibit soon after excision a reversed or downward current.

During excitation the upward current undergoes a diminution in the case of muscle or of nerve, an augmentation in the case of the eyeball.

I shall not dwell on the first two cases, they are only presented as affording standards of comparison with the third case, that of the eyeball.

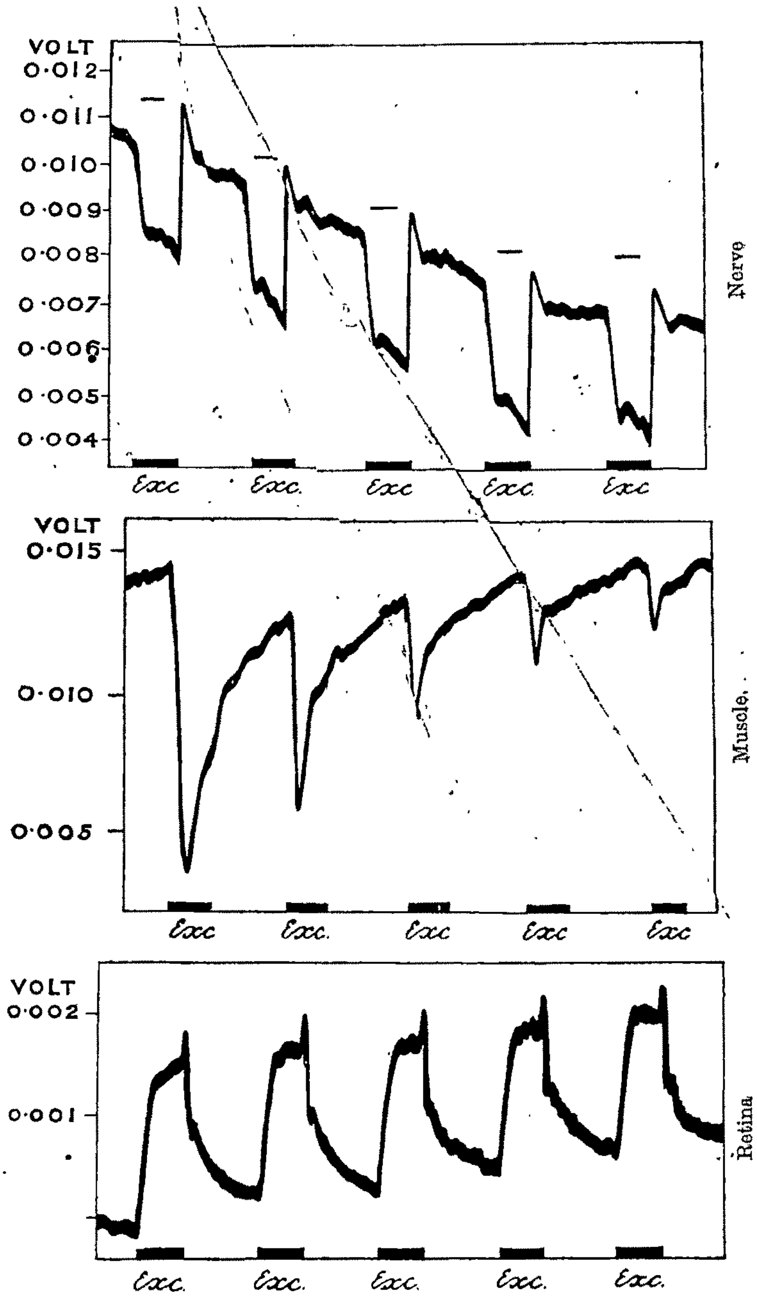
There are two obvious points in the comparison :—

(1) Fatigue, as evidenced by the diminishing maximal effects of a series of maximal excitations, most obvious in the case of muscle, not obvious at all in the case of nerve, is only moderately well marked in the case of the eyeball.

(2) The effects of excitation are negative in the case of muscle and nerve, positive in the case of the eyeball.

Both these points require some comment.

(1) The conditions of observation in the three cases are not strictly identical. In the first two cases the excitation has been electrical, in the third it has been a stimulation by light. I have not yet succeeded in obtaining for comparison



Figs. 6, 7, and 8.

Currents of action of nerve, of muscle, and of retina.

In each case the excitation lasts for one minute, and the subsequent period of rest for two minutes. There are five periods of excitation in each series. The nerve is excited by tetanising shocks; the muscle is excited by tetanising shocks of its nerve; the retina is excited by exposure to candle-light.

The nerve record exhibits a series of undiminishing negative variations.

The muscle record exhibits a diminishing series of negative variations.

The eye record exhibits a slightly diminishing series of positive variations.

a series of retinal responses by electrical excitation.[1] It seems to me, however, that the comparison now made is a permissible one, the retina having presented to us a series of maximal effects by maximal stimulation by light. Such being the case, we may comment upon the remarkable endurance of the response, and express the opinion that such endurance is due not to insignificant chemical disintegration during activity, but to considerable and effective chemical reintegration during repose, and, it may be, during activity itself. I am of the opinion, on grounds that I hope shortly to make clear, that reintegration of retinal matter sensitive to light, goes on during its disintegration by light, as well as during darkness—that during activity retinal exhaustion is prevented by retinal invigoration. I shall return to this point presently.

(2) The fact that the retinal response is positive, whereas the responses of muscle and of nerve are negative (to the original upward current of rest of fig. 5), has not quite the simple significance that might at first sight be attributed to it. The actual direction of current of rest in the eyeball is unessential to the direction of the current of illumination; the former may be positive or negative, whereas the latter, which is the essentially interesting effect, is in general positive. It is advisable for any clear understanding to consider the latter without any reference to the former, and to realise its direction through the layers of the retina. If we consider an eyeball in its natural position, with cornea facing the sky and optic nerve stump to the ground, the direction of our current is upwards from the choroidal or pigment layer of the retina to its vitreous or nerve-fibre layer, and to be represented by an arrow pointing upwards from fundus to cornea—as we fancy we look at things—and thereafter through the galvanometer completing circuit from cornea to fundus. I usually take as my working mnemonic in the laboratory that the retinal response of an eye looking at the galvanometer "looks through" the latter. Where shall we look for the motive force driving our imaginary arrow? I think at the rod and cone layer of

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[1] Note 8, p. 35.

the retina, where therefore you may picture as placed the tail of the arrow, the part to which the tense bowstring of photo-excitable stuff is applied and liberated by the stimulus of light. But let me repeat that we are to conceive that two simultaneous and opposite movements are promoted in the retina by light—the winding-up process by which potential energy is stored, the running-down process by which active energy is liberated.

I alluded to the grounds on which this view is based; let me now briefly expose these grounds.

The positive electrical effect of retinal illumination is assuredly not a single simple phenomenon, but a compound effect—the resultant of simultaneous and antagonistic forces. Being antagonistic, such forces must be conceived as two in number, or at least in two opposite camps if the components ultimately discovered should prove to be more than two. But however numerous such components might prove to be, they could not take effect otherwise than in one or other of two directions, which we shall therefore distinguish as positive and negative.

The signs by which we may recognise that the positive electrical effect of retinal illumination is double, are apparent at the commencement and at the end of prolonged illumination—at "make" and at "break" of light.

The main or principal effect *during* illumination is positive, and this positive effect gradually subsides during obscurity. Usually the initial effect at the commencement of illumination, *i.e.*, at *make* of light, is positive, but occasionally it is distinctly negative, and sometimes it is doubtful to an observer whether the very first motion of the galvanometer spot is negative or positive; sometimes again it is distinctly positive, then negative, before passing into the enduring positive position it takes up during illumination.

At the end of illumination the subsidence of the positive deflection is always preceded by a more or less well-marked sharp positive augmentation, *i.e.*, at *break* of light there is a sharp augmentation of the positive deflection during light, followed by gradual subsidence to the obscurity level.

One's first thought in presence of this somewhat puzzling break effect, is that the main positive effect during illumination may be a sign of pigment activity, while the terminal positive effect at break of light may be due to a movement of the cones. But on this view it is difficult to account for the fact that the terminal effect, if due to relaxation of cones, has not always its distinct initial counterpart at make of light by reason of a contraction of cones. I therefore hesitate to offer this in explanation of the facts, and shall content myself with the demonstration of the presence of two simultaneous and opposite effects, without committing myself to an assertion that such opposite effects have their seat in the same or in different retinal elements.

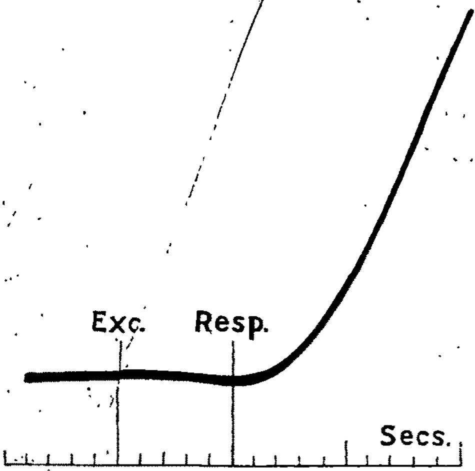


FIG. 9.

Eyeball of the second stage with a "period of hesitation" lasting five seconds.

The lost time of these make and break effects, more especially of the former, *i.e.*, the time elapsing between the commencement of illumination and the commencement of deflection, is highly significant of the double nature of the chemical change of which the electrical change is the outward and visible sign.

As regards the make effect in particular, or rather the practically simultaneous make-break effect of a flash light, the interval between stimulus and deflection is physiologically enormous, obvious to simple observation as quite a long pause, and not requiring therefore a very rapidly travelling plate for its photographic registration.

We evidently have to do, not with a simple period of latency,—such physiological inertia in the case of the retina is simply incredible—but with what I shall characterise as a period of hesitation, during which a tug-of-war, so to say, is taking place in the retina between two opposite forces or processes, positive and negative, that for a period counterbalance each other in the circuit.

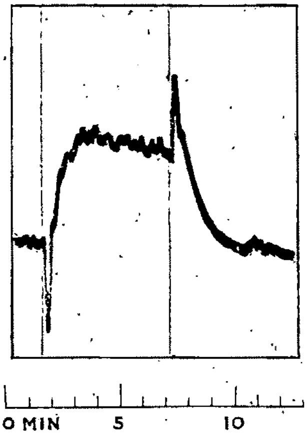


FIG. 10.

An old record of the retinal response to light (June 4, 1895; Candle at 2 feet = 25 units), which, although not of the usual type, I then regarded as being normal. In a sense it is so, but only for an eyeball in the second stage, as described in the text.

A similar if less pronounced opposition of forces occurs at the end of illumination, when the two forces cease to act. But whereas we must suppose that at make of light, both forces commence to be evolved at almost equal rates, and that during light the positive force is the stronger, we must admit that at break of light, negative ceases more suddenly than positive, so that a short positive *plus* precedes the more gradual positive *minus*. And if from any cause there should have been during the period of hesitation at make of light a sufficiently marked superiority of negative over positive, then we shall witness at make of light a distinct negative effect preliminary to the main positive effect—as shown in fig. 10.

The record, which was taken in July, 1895, was obtained on an eyeball in the second or transitional state, and Professor Kühne, when I showed it to him, recognised at once that it was the response of a partially-injured eyeball. The hint was not lost upon me. On returning to the subject last year I paid particular attention to the transitional types that are observed. And since I have mentioned Kühne's name in this connection to acknowledge a valuable hint, I should like to take the opportunity of showing you how closely some of my photographic records of 1899 reproduce the plotted curves of Kühne and Steiner of 1881. I have confronted in the two halves of fig. 11 Kühne and Steiner's fig. 1, which they give as representing the usual course of events in the isolated retina, and one of my own records of a response of an eyeball in the second stage. The similarity is sufficiently obvious.

That this is a reasonably probable view to take of the case is confirmed by the alterations of effect taking place in an eyeball accidentally mishandled, or left to become partially dry upon the leading off electrodes. From the freshly-prepared state, with an eyeball at its best, to the moribund state with an eyeball at its worst, I distinguish three stages.

In Stage I. the deflection at make of light is at once positive, the deflection during illumination is positive and increasing or stable; the deflection at break of light is positive and small, followed by gradual decrease of the main positive deflection to the normal obscurity level.

With lapse of time the main positive effect is less and less sustained during illumination, and the terminal deflection at break is relatively large. The deflection at make of light becomes "hesitant," being sometimes frankly

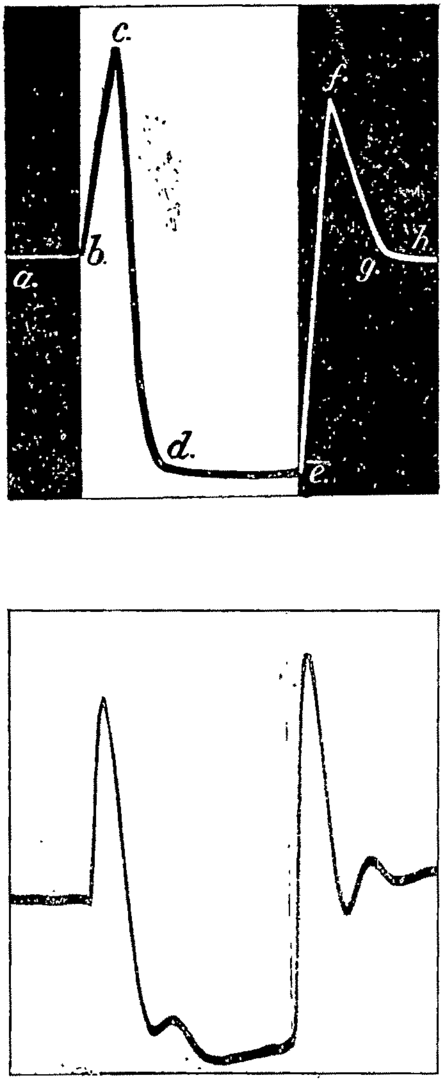
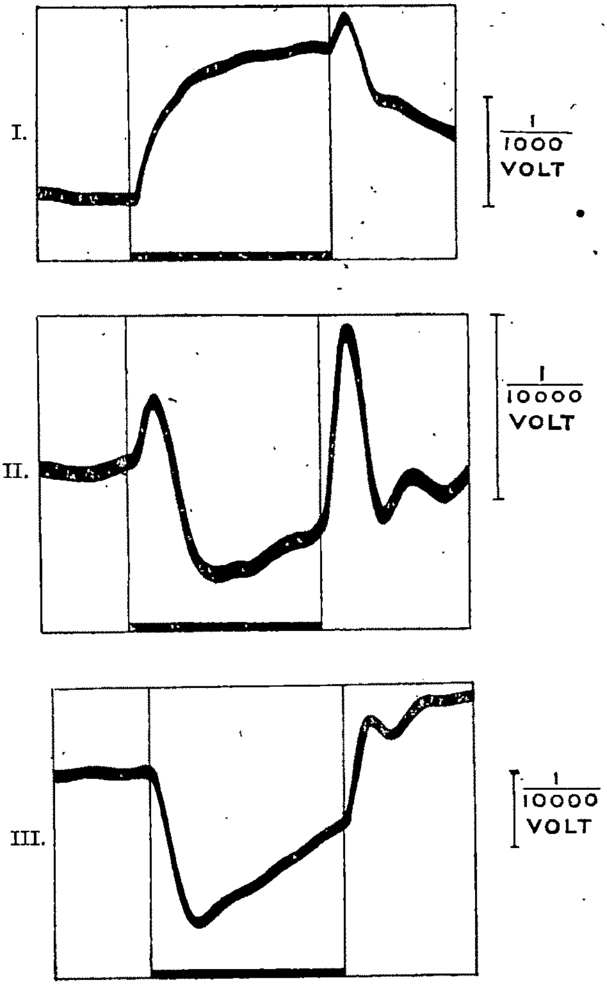


FIG. 11.

Comparison between Fig. 1 of Kühne and Steiner's second paper on retinal currents (1881) and a record of retinal response of the second stage, as described in the text.



Figs. 12, 13, and 14.

Electrical responses to illumination of the retina in the three stages described in the text.

(I.) Fresh eyeball. Considerable and augmenting positive effect. Small terminal positive increment.

(II.) Eyeball about six hours after excision. Initial positive effect followed by prolonged negative effect. Large terminal positive deflection.

(III.) Eyeball about twenty-four hours after excision. Clear negative effect during illumination.

In each case stimulation is made by exposure lasting one minute to a standard candle 2 feet from the eyeball.

(Fig. 8 is the continuation of Fig. 12, recorded from the same eyeball on a more slowly travelling plate.)

negative, sometimes positive with negative interruption, sometimes positive after a long period of hesitation.

In Stage II. the main positive deflection has disappeared, the state during illumination being neutral or actually negative. At make of light the deflection is positive, and markedly "hesitant." The terminal deflection at break of light is positive and large, being, in fact, the most prominent feature of the sequence.

In Stage III. the deflection is negative throughout illumination; at make the deflection is frankly negative, during light it is decreasingly negative; at break the deflection is positive, and the spot returns to its normal level of obscurity.

An even cursory review of these three stages, taken in conjunction with the peculiar period of hesitation at make of light, must reinforce the view that we are in presence of a double process, and that the dominantly positive effect of Stage I. has latent in it the opposite negative effect that is wholly unmasked in Stage III.

I have sought in many ways to separately influence the positive and negative effects—by drugs, by strong electrical currents, by raised temperature, by increased eyeball tension—acting on the supposition that by partial injury I might be able to, so to speak, wipe out the presumably more delicate process of constitution, and thus unmask the more enduring process of destitution. I find that the best and almost unfailing means of doing this is to partially injure the retina by compression of the eyeball. For an effective lecture demonstration, a fresh eyeball, giving the regular positive effect on illumination, may be taken off the electrodes, moderately compressed and rolled between the fingers, and replaced upon the electrodes; the effect of illumination on this massaged eyeball will almost certainly be negative.

Colour antagonism?

One may hardly be expected to make even the most cursory survey of positive and negative retinal changes without allusion to the comparative effects of the several colours that make up white light—with reference of course to the well-known antagonism theory of Hering, white *v.* black, red *v.* green, yellow *v.* blue, which has played such a prominent part in the literature of colour-vision. We have seen that there is a very clear antithesis as regards the retinal effects of light and darkness, so that we might perhaps say that white and black are antagonists, and that white provokes an action while black promotes an opposed reaction. Can any similar antithesis be recognised between the two "dissimilative" colours red and yellow and the two "assimilative" colours green and blue, which, on the antagonism theory, are regarded as promoting opposite chemical changes in the retina?

On trial of this point we find in all cases that different colours give rise to electrical effects in one direction, though of varying magnitude. The order of efficacy in my own trials, made with carefully selected coloured glasses, has been:—red, blue, green, yellow, white, *i.e.*, in a sense that is obviously governed by luminosity. To quote an instance, the deflections were

With Red	+ 4
Blue	+ 9
Green	+ 12
Yellow	+ 16
White	+ 33

Stimulation at 25 units. Illumination for 6 seconds at 1 minute intervals.

But we at once object that a possible opposition between the purely chromatic constituents has, perhaps, been masked by the white-valency common to all the colours, or by white light passing through the imperfect colour filters.

We therefore make two further series of trials (1) to learn whether the joint effect of two opposed colours is greater or smaller than their separate effects; and (2) to learn whether the separate effects of any two opposed colours are equally or unequally altered when the retina has been submitted to prolonged modification by one of the two colours.

I find (1) that taking two very weak colour stimuli, *e.g.*, red and green, the conjoint effect of both stimuli is always greater than either of the separate effects, and not far short of their sum ; (2) that a retina subsequent *e.g.*, to prolonged green stimulation or to prolonged red stimulation, exhibits equal fatigue to green and to red stimuli.

Here are two representative experiments—

I.

Red alone	+ 5
Green alone	+ 10
Red + Green	+ 14
White	+ 40

Stimulation at ¼ unit.

II.

Red	+ 21
Green	+ 28

Ten minutes' exposure to Green.

Red	+ 16
Green	+ 24

Ten minutes' exposure to Green.

Green	+ 22
Red	+ 15

Ten minutes' exposure to Red.

Green	+ 20
Red	+ 12

Ten minutes' exposure to Red.

Red	+ 8
Green	+ 18

Stimulation at 100 units. Lasting 10 seconds.

But for my own part, I must confess that I do not attach much value to these colour experiments. They are made upon the frog's retina; we have no reason to think that the frog is at all a judge of colour; the results show at most that the hypothetical chemical antagonism of colours is certainly not any deep-seated physiological antithesis pertaining to all retinal matter "excitable" by light. The psychologist remains as free as ever to believe or not to believe that the perception of colour by the human brain is three dimensional, and depends upon disintegration-cum-reintegration of a white-black substance, and of a red-green substance, and of a yellow-blue substance. But this to my mind is a psychological chemistry, and I do not wish to wander too far afield from a physiological base.

Let me bring this chapter to a close by referring briefly to the positive and negative electrical effects that are manifested by ordinary nerve. The three stages just described as regards retinal effects, and the very probable double character of such effects, recall to mind the somewhat similar series of effects in freshly isolated dying nerve. Only whereas the three stages that I described in the case of nerve refer to electrical effects of electrical excitation, the retinal series refer to electrical effects of luminous stimulation.

The electrical response of isolated nerve tetanised by alternating currents is with lapse of time:—(1) a simple negative effect; (2) a negative effect immediately followed by a positive after effect; (3) a positive effect. Nerve in the second stage seems to be most clearly suggestive of the operation behind the scene of two opposite processes of action and reaction, of which the prominent manifestations in this case are successive. It would appear, moreover, that there is some kind of analogy between the early positive and late negative effects in retina on the one hand, and the early negative and late positive effects in nerve on the other hand, but I should be very unwilling to speculate very far along this superficial and obvious analogy. We may, however, consent to speculate in moderation, and admit that just as in the retina there is a store of matter that is formed, and that is consumed under the excitation by light, so in nerve there is analogous stored matter formed by activity and subserving activity.

Significance of the Medullary Sheath. Fatigue of Non-Medullated Nerve.

Naked gray matter, as of a nerve centre, is very rapidly exhausted, and has to be replenished at leisure from the nutritive fluids. Protected gray matter, as the conductile axis of medullated nerve-fibre, is extraordinarily inexhaustible because its wear and tear of action is instantly effaced by the restorative reaction of its white envelope; just as the highly mobile elements of the retinal organ, provoked to action and therefore to expense by light, are *pari passu* kept supplied and protected from exhaustion out of the store of pigment that is our visual inogen.

It is by action and reaction between core and sheath that the nerve-impulse is propagated along a medullated nerve-fibre. It is by the same action that the impulse is insulated within a definite conducting fibre. And by the same means there is secured to the essential part—the grey core—an almost instantaneous restoration of expended matter necessary to unimpaired function rapidly repeated.

Do we ask for evidence of a commerce of matter between the grey core and its white jacket of phosphorised fat? We have such evidence—and of the most cogent—in the first gross fact of Wallerian degeneration. The grey core of a nerve-fibre is the arm of a nerve-cell which is its body, and when the nerve is cut the arm degenerates away from the body. The first and most obvious change of structure takes place, not in the core itself, which was in continuity with the cell body, but in the discontinuous sheath, by which it is enveloped and nourished. The disordered nutrition of the principal part—the axis, is first visibly manifested by the superadded and subordinate part—the sheath.

If this hypothesis be well founded, we should expect that non-medullated nerve, examined as to exhaustibility, would be found to conform to the type of exhaustible muscle rather than to the type of inexhaustible nerve.

Miss Sowton, who at my request has investigated the point upon the olfactory nerve of the pike, has as a matter of fact found this to be the case.

Veratrine and Protoveratrine.

Veratrine, $C_{32}H_{49}NO_9$, and protoveratrine, $C_{32}H_{51}NO_{11}$, are two closely related alkaloids derived from green and from white hellebore respectively. The former, as is well known, has a specific action upon muscle, and causes its contraction to be extraordinarily prolonged. A veratrinised

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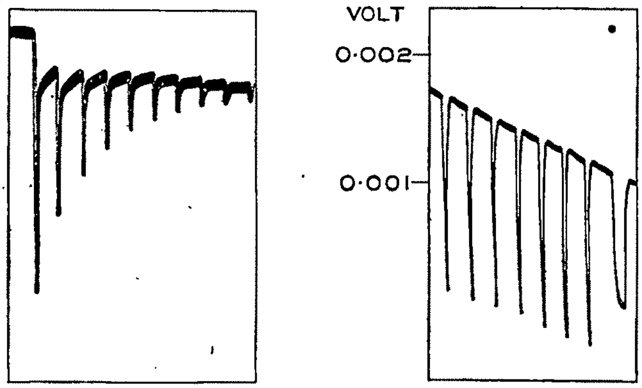
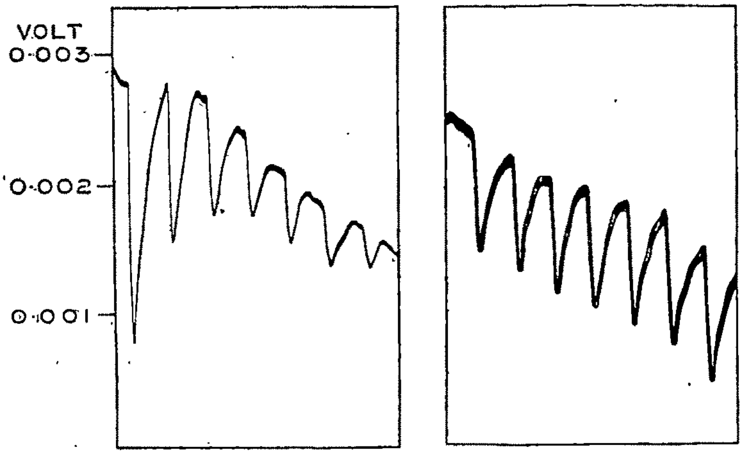
muscle contracts vigorously but does not relax. Pure veratrine has comparatively speaking no action upon nerve.

Protoveratrine, which has recently been identified and distinguished from veratrine by Boehm, has a specific



Muscle. Nerve (medullated).

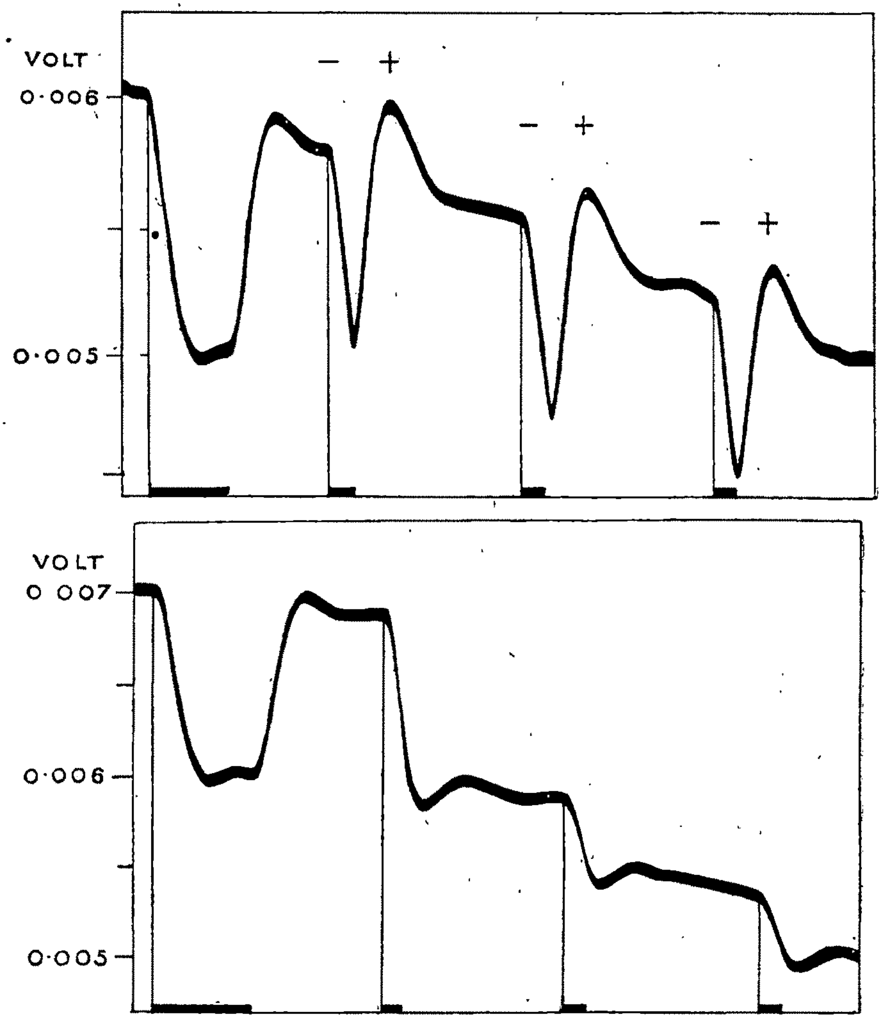


Nerve (non-medullated). Retina.

FIGS. 15, 16, 17 AND 18.

Portions of records of ordinary muscle, of medullated nerve, and of non-medullated nerve (olfactory nerve of pike) similarly excited—to show that non-medullated nerve resembles muscle and differs from medullated nerve, as regards the manifestation of fatigue.

Fig. 18 is a similar retinal series of responses to light, exhibiting little or no sign of fatigue (retina of the third stage).



FIGS. 19 AND 20.

To illustrate the contrast between veratrine and protoveratrine.

In each case a frog has received an injection of one drop of a ½ per 100 solution of the alkaloid (=about 0·0005 gramme, *i.e.*, a very large dose). Between ½ and one hour later the apparently dead frogs have been pithed and a sciatic nerve of each has been removed and placed upon the electrodes.

In each case three electrical responses (at intervals of one minute to tetanisation lasting for six seconds) have been recorded.

The three veratrine responses are normal and undiminishing; each response exhibits a negative effect during excitation and a positive effect after excitation.

The three protoveratrine responses are sustained and diminishing; each response exhibits a negative effect during and after excitation.

The deflection to the left of each record is a standard deflection made by passing current from $\frac{1}{1000}$ volt through nerve and galvanometer. It serves to give the voltage scale of the nerve-responses, and shows to what extent the galvanometer is "dead-beat."

action upon nerve, and comparatively speaking no action upon muscle. It causes the negative variation of excited nerve to be extraordinarily prolonged. The fact in itself is of considerable interest, inasmuch as it is at present a solitary and very clear case of two drugs, closely allied chemically, and having each a sharply defined predilection for muscle or for nerve. Veratrine acts upon muscle. Protoveratrine acts upon nerve. And the action of protoveratrine upon nerve is very similar to the action of veratrine upon muscle. Just as in muscle veratrine impedes the relaxation of a contracted state, so in nerve protoveratrine impedes the positive reaction that is normally associated with, or consequent upon, excited activity. Normal nerve gives during excitation a negative variation that signifies disintegrative change, and after excitation a positive return to, or it may be beyond, the normal level of a quiescent state, signifying reintegration. Veratrinised nerve acts and reacts normally. Protoveratrinised nerve exhibits a well-marked negative sign of action during excitation, but little or no positive sign of reaction after excitation. And in correspondence with this failure of positive reaction, the succession of action-effects exhibits rapidly progressing exhaustion. A succession of negative variations of normal (or of veratrinised) nerve, exhibits from first to last little or no diminution. Successive negative effects on protoveratrinised nerve are permanent and rapidly diminishing. Exhaustion is apparent in medullated nerve when its positive process of restitution is impeded.

III.—The Law of Reaction.

The simplest problem that we may set ourselves to resolve in the case of any excitable tissue—such as muscle, nerve or retina—is to determine how much responsive effect follows upon how much exciting cause.

And we shall most conveniently summarise our results by plotting a curve, marking off magnitudes of cause (= excitation) along the X axis and magnitudes of effect along the corresponding ordinates parallel with the Y axis.

Taking, for example, a series of stimuli of arithmetically increasing magnitudes, 1, 2, 3, 4, 5, and having determined that the corresponding effects come out at the magnitudes 34, 58, 72, 82, 90, the cause-effect curve plotted out on this principle would be thus:

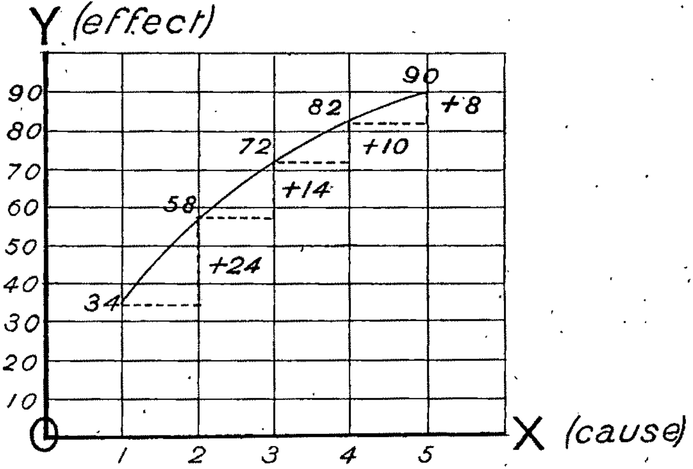


FIG. 21.

Curve exhibiting the electrical response (Y) of the retina to luminous stimulation (X) of arithmetically increasing magnitude (energy). The unit of light in this case is $\frac{1}{100}$th part of the light of a standard candle at a distance of 1 foot, *i.e.*, the light of a standard candle at a distance of 10 feet.

viz., concave to the abscissa OX, and exhibiting at a glance that + 24 + 14 + 10 + 8, diminishing increments of effect, are caused by equal increments of excitation.

Now let us plot out the results of an actual experiment in which the cause was luminous stimulation, and the effect an electrical response of the retina.

The X series was 1, 2, 4, 6, 8 units.

The Y series was 44, 60, 68, 72, 75 degrees of scale.

The plotted curve is obviously concave towards the abscissa OX, *i.e.*, equal increments of luminous excitation cause diminishing increments of retinal change.

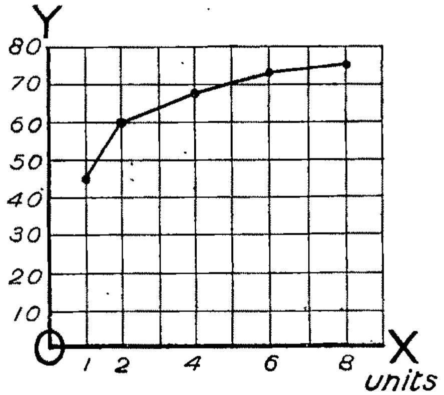


FIG. 22.

Curve exhibiting the electrical response (Y) of the retina to electrical stimulation (X) of arithmetically increasing electrical energy (condenser discharges).

Let us take as another illustrative instance an experiment in which the cause was electrical stimulation and the effect a subsequent electrical response of the retina.

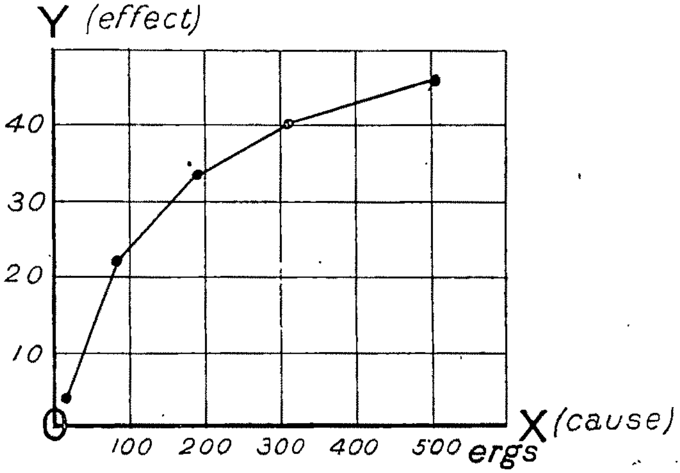


FIG. 23.

The X series was 20, 80, 180, 320 and 500 ergs.
The Y series was 4, 22, 34, 40 and 45 degrees of scale.

As before, the cause-effect curve is concave to the abscissa OX, *i.e.*, equal increments of cause produce diminishing increments of effect.

The cause-effect curve of stimulation and sensation, as expressed by the logarithmic law, is of a precisely similar type, *i.e.*, equal increments of sensation require increasing increments of stimulation, or otherwise expressed, diminishing increments of sensation are produced by equal increments of stimulation. Taking, *e.g.*, intensity of light along the X axis, and intensity of sensation along the Y axis, we require geometric increase of X to produce arithmetic increase of Y, or otherwise expressed, arithmetic increase of X produces logarithmic increase of Y.

This well-known and much criticised law of sensation, which with reservation may be admitted to be the fundamental law of psychophysics, holds good only within certain limits of moderate stimulation. Within the moderate range of ordinary daily sensation, it is obviously reasonable that equal increments of stimulation should effect decreasing increments of sensation, and that all sensation should find its limit with maximal alteration of nerve-matter. Between objective stimulus and subjective consciousness we have to consider physiological change of nerve-matter, of which change of consciousness is the symptom. An external stimulus X arouses physiological change of nerve-matter Y, which material change or internal stimulus Y is the basis of the sensation Z. Firstly, external stimulus, secondly, physiological change, thirdly, sensation—a relation between first and third such that equal increments of the former arouse decreasing increments of the latter. Is this limitation of effect, which is so clearly pictured in the concave curve, a limitation of physiological change Y producible by stimulation X, or a limitation of psychical change Z producible by physiological stimulation Y? Clearly, I think, the former—since we find in the case of the retina, or indeed in any case where the physiological effects of excitation are experimentally accessible, that equal increments of excitation arouse diminishing increments of physiological effect.

Less clearly, and with less confidence, yet, I think, with some degree of justification, we may assume, at least for the sake of clear thinking, the corollary to this conclusion, viz., that there is no disproportion between the physiological change *Y* and the psychical sensation *Z*, *i.e.*, that equal increments of sensation belong to equal increments of physiological change; or, again, that the symptom felt is the true arithmetic measure of the physiological state of nerve-matter which is its basis.

Let us consider rather more closely the two extremes of minimal and maximal sensation.

With indefinite increase of stimulation it is clear that we cannot have indefinite increase of physiological change, nor, therefore, indefinite increase of sensation. There must be a maximal effect. All change in living matter is, indeed, self-limitative; the activity of all living matter expends itself, and is arrested by the products of activity; with excessive stimulation the curve of sensation ceases to rise and then falls away from its maximum, losing itself finally in some other kind of sensation, or in actual anæsthesia through mere physiological exhaustion of nerve matter. Does such blunting of sensation come to pass through the agency of waste-products of excessive activity, of which carbonic acid is the representative? We may imagine so, but we may hardly say so.

At the lower end of the scale, down near the threshold of sensation, it is hardly reasonable to expect that a concave curve, constructed on the same formula as that, expressing the relation between moderate stimulation and moderate sensation, should express the relation between minimal stimulation and minimal sensation. Such a curve, steepest at its commencement, *i.e.*, with greatest increments of Y for given equal increments of X, would signify that close to the threshold absolute differences of X of infinitesimal magnitude take effect upon consciousness, *i.e.*, a condition of extraordinary hyperæsthesia towards the minutest stimuli of our environment.

We should expect to find, and in point of fact we do find by careful experiment, that the minimum perceptible difference, *e.g.*, of light, is a considerably higher fraction at low intensity than at moderate intensity, *e.g.*, 1 in 5, or 1 in 10 at low intensity, as compared with 1 in 50 or 1 in 100 at moderate intensity. We all know indeed that it becomes more and more difficult to see print distinctly with fading light. This signifies that we are relatively less sensitive to differences of weak light, relatively more sensitive to differences of moderately strong light—in other words, that the early rise of the curve from the threshold is by increasing increments of sensation, *i.e.*, convex to the abscissa. A curve beginning thus, convex to the abscissa, and subsequently becoming concave to the abscissa, may be briefly designated as an S-shaped or sigmoid curve. To say that the cause-effect curve (cause measured along the X axis, effect along the Y axis) is a sigmoid curve, is to say in brief that equal increments of cause from minimal to maximal produce at first increasing increments of effect, and subsequently decreasing increments of effect. Fig. 24 is intended to make this point clear.

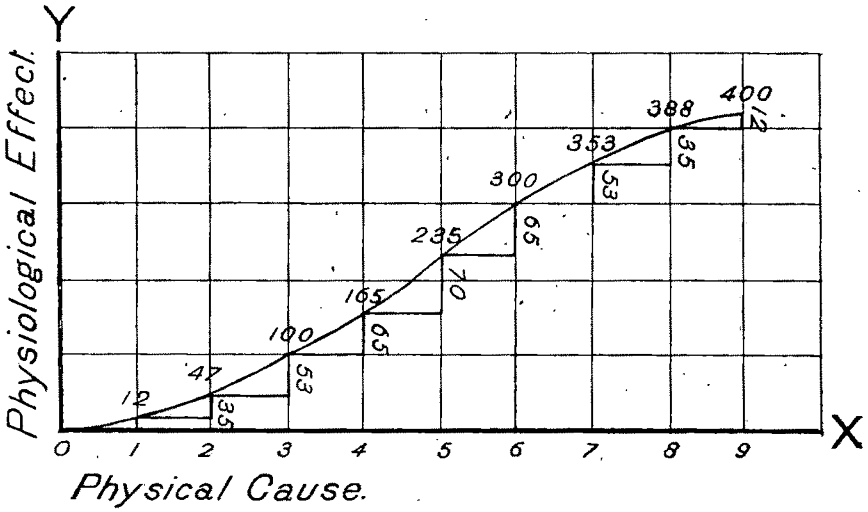


FIG. 24.

Curve exhibiting the electrical response (Y) of the retina to luminous stimulation (X) of low arithmetically increasing intensity (energy). The unit of light is here one quarter of the unit taken for Fig. 21, *i.e.*, the light of a standard candle at a distance of 20 feet.

I consider that a sigmoid curve as just defined gives graphic form, not merely to the relation between physical excitation and psychical sensation, but to the general relation between physical cause and physiological response in the excitation of living matter, of nervous matter, and in particular of the retinal substance excitable by light.

I look for, and find it, in the case of muscle, and in the case of nerve, and in the case of the retina, and venture to speak of it as the law of reaction.

A comparatively rough series of trials suffice to bring out data that are plotted in a curve concave to OX, *i.e.*, with diminishing increments of effect to equal increments of cause.

A more delicate series of trials, with stimuli of low intensity and increasing by smaller increments, is necessary to bring into evidence the initial convex portion which is comparatively short.

Fig. 25 is a good example of it upon the retina, strength of light being plotted along the X axis, magnitude of electrical response along the Y axis.

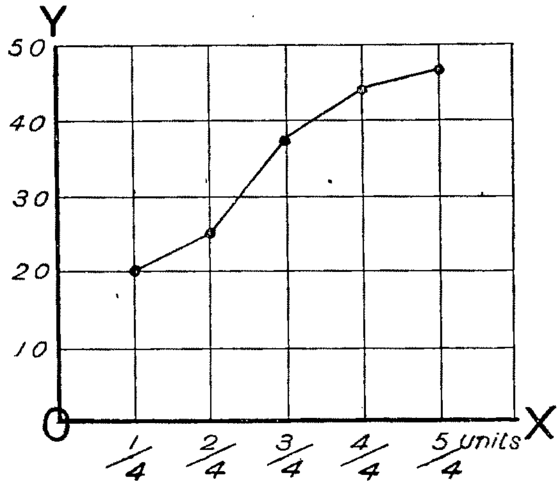


FIG. 25.

Let me try to illustrate the great general significance of a sigmoid curve, such as I have urged as symbolising more faithfully than the wholly logarithmic curve the law of physiological reaction, which I take to be inclusive of the law of psychical reaction.

The adequate performance of any human task is the effect of human energy—How much energy X to how much result Y in the asymptotic approach towards perfection?

In, let us say, the learning of a language, we know that the first steps cost much, and that the effect rises slowly; then the upward progress becomes more rapid, successive equal increments of energy give successive increasing increments of knowledge; finally progress slackens, the last steps towards perfection cost energy far in excess of those taken within the range of mediocrity.

The easiest part of any task, that in which the smallest effort seems to give greatest progress, is its middle portion; the two hardest and most expensive parts are its beginning and its end.

NOTES AND REFERENCES.

(1) Inexhaustibility of Nerve-Fibre (p. 5).

I have insisted upon this point upon more than one occasion—for the first time in 1885 and in 1886 in two successive reports to the Scientific Grants Committee of the British Medical Association (*B. M. J.*, July, 1885, and July, 1886), for the second time in 1891 in a paper on the "Sense of Effort," communicated to the Neurological Society (Brain, 1891, pp. 179-433), and for the third time in the Croonian Lecture for 1896 (*Phil. Trans. R. S.*, 1897).

Wedensky in 1883 (*Cbt. f. d. Med. Wissenschaft*) and Bowditch (*J. of Physiology*, 1885; *Du Bois-Reymond's Archiv.*, 1890), came to the same conclusion, viz., that nerve-fibre is practically inexhaustible, and expressed themselves far more unreservedly than I then did, or should care to do now. The negative variation of nerve is an ultimate sign of life, and even if electrotonic effects are excluded, is not a safe proportional indicator of the capacity for function which requires not merely a living state, but a living state of high excellence. A nerve that can conduct nerve-impulses will certainly manifest a negative variation, but it does not follow that a nerve that will manifest a negative variation is capable of conducting nerve-impulses.

I share the opinion expressed by Pflüger to the effect that the negative variation is itself proof positive of a chemical change in active nerve, that activity if long enough and strong enough *must* cause chemical expenditure, and, therefore, fatigue. But the anomaly of apparent inexhaustibility of nerve in the presence of undeniable chemical change, is in my view reconciled when we have recognised the extraordinary rapidity with which exchange of matter is effected between gray axis and white sheath. I regard the white sheath as forming a store of nutrient matter surrounding the gray axis—feeding it and fed by it—enabling the function to be performed, and itself a secondary deposit aroused by the function. In short, I regard medullated nerve as supplying a striking case of "complementary nutrition"—of that "consensus partium" between two mutually interdependent tissues according to which waste matter of each tissue is raw material to the other tissue.

(2) FATIGUE OF THE END-PLATE (p. 5).

In the illustration given in the text the effect on muscle has been produced by excitation of its nerve, and the decline is, therefore, by progressive fatigue of the end-plate.

This point was established in my reports to the Scientific Grants Committee of the British Medical Association for 1885 and 1886 (*B. M. J.*, July, 1885, and July, 1886), when I compared the state produced by fatigue and by nerve-degeneration with that produced by curarisation, and formulated the conclusion that the motor end-plate is the weak link in the neuro-muscular chain, being the point at which the function of transmission is first affected with excess of action, or with disordered nutrition or with the onset of death, just as in curarisation.

In voluntary action—involving changes throughout the tract from Rolandic cell to periphery—the chiefly fatiguable points are presumably the cells or points denuded of white matter, viz., the cerebral cell, the spinal cell, and the motor end-plate. I have elsewhere formulated the law that fatigue effects declare themselves with diminishing gravity from centre to periphery, *i.e.*, that central fatigue is limitative of peripheral fatigue.

(3) ISOLATED NERVE AS A TEST-OBJECT (p. 5).

The general application of the electrical method to the pharmacodynamics of isolated nerve was first broached and described in a series of three papers communicated to the Neurological Society in 1896, and published in BRAIN, 1896, pp. 43, 277, and 569.

The particular case of carbon dioxide is considered at length in the Croonian Lecture for 1896 (*Phil. Trans. R. S.*, 1897).

Other developments of the same subject are contained in the Proceedings of the Royal Society and of the Physiological Society for the years 1895 to 1899.

The fundamental principles of the method are given in my "Lectures on Animal Electricity," 1897.

(4) THE AXIOM OF GENERAL PHYSIOLOGY, p. 7.

The expression is of Claude Bernard (*Phénomènes de la Vie*, 1879, vol. ii.).

"On peut distinguer deux ordres de phénomènes :—

"(1) Les phénomènes de fonctionnement, ou encore d'usure, ou de *destruction vitale.*

"(2) Les phénomènes de formation, ou de création vitale, ou encore de *synthèse organique*. . . .

"Les deux types ne sont jamais isolés ; ils sont indissolublement connexes, et la vie de quelque être que ce soit est charactérisée précisément par leur réunion et leur enchaînement ; ils représentent les deux phases du travail vital.

"Cette vérité constitue, ainsi que nous l'avons dit ailleurs, *l'axiome de la physiologie générale*. On peut être assuré que toute doctrine qui serait directement ou indirectement en contradiction avec cette donnée fondamentale est fausse, et que le principe de l'erreur est précisément dans cette contradiction."

(5) POSITIVE AND NEGATIVE (pp. 8 & 9).

It is purely matter of convenience and convention which of two opposed movements we may choose to designate as positive and which as negative. But once having made our choice, the convention must be adhered to throughout the course of any given argument.

As regards muscle, the usual custom is to regard contraction as the positive act, relaxation as the negative act.

As regards the chemical changes, however, we are naturally led to take negative change (katabolism) as the chief feature of contraction, and to regard positive change (anabolism) as the reaction during relaxation.

As regards the electrical change, it is usual to refer to the poles of the external circuit, and not to the electro-motive elements. On this understanding the pole connected with active tissue is negative, just as the pole connected with the zinc of a voltaic couple is negative. In physiological literature active tissue is termed negative, whereas in physics the zinc carrying the negative pole is termed electro-positive.

I venture to think that the electro-motive action of active tissue is more vividly pictured when referred to an electro-positive element as the driving force, than when it is indicated by negative pole. Moreover, the latter custom introduces misleading expressions, such as "active tissue electro-negative to normal tissue," "negativity of action," &c.

Physiologically *active* tissue, in which presumably disintegrative exceeds reintegrative change, like the zinc of voltaic couple, is *electro-positive*, and its external pole is *negative*. Physiologically *quiescent* tissue, in which presumably reintegrative exceeds disintegrative change, is *electro-negative*, and its external pole is *positive*.

In any case, where there is danger of ambiguity from the terms positive and negative, direction of current should be clearly indicated by words or by diagram.

(6) Retinal Response to Light (p. 9).

The variation of current of the illuminated eye was discovered by Holmgren in 1871 (*Cbt. f. d. med. Wiss.*, 1871, p. 423), and further investigated in 1873 by Dewar and McKendrick (*Trans. R. S. Edin.*, 1873, p. 141; *Journ. of Anat. and Physiology*, vii., p. 275, 1873), and in 1880-81 by Kühne and Steiner (*Unters. a. d. physiol. Inst.*, Heidelberg, vols. iii. and iv., 1880-81).

Holmgren described the retinal response to light as being positive in the case of the frog, negative in the case of mammals.

Dewar and McKendrick sum up their observations on the frog's eye as follows:—"The natural electro-motive force is in the first place increased, then diminished; during the continuance of light it is still slowly diminished to a point where it remains tolerably constant; and on the removal of light there is a sudden increase of the electro-motive power nearly up to its original position."

Kühne and Steiner in their second paper (*Sehorgan*, 1881) give an account of retinal phenomena in many respects similar to that which I have given in the text, of the successive changes as they came under my observation. K. and S. insist particularly upon the permanently positive response of the normal eyeball and upon its alterations by injury. They consider the negative effect to be produced by partial detachment of the retina, and the positive effect during illumination to be the expression of a regenerative influence of the retinal epithelium.

These and other points will be more fully discussed in a paper that I am now drawing up for communication to the Royal Society.

Quite recently (November, 1899), Beck has described the retinal response of the cephalopod retina as positive (*Pflüger's Archiv.*, vol. lxxviii., p. 129, 1899).

(7) LATENCY OF THE RETINAL RESPONSE (p. 12).

Dewar and McKendrick made the first approximate measurements of latency, and found it to be not more than $\frac{1}{10}$th sec.

S. Fuchs (*Pflüger's Archiv.*, vol. lvi., p. 408, 1894), with the aid of Bernstein's rheotome, measured it as being 0·0004 to 0·006 sec.

(8) TETANISATION OF THE RETINA (p. 8).

I have since made the experiment alluded to in the text. The results are altogether similar to those obtained by illumination. Alterations of retinal excitability are manifested in a nearly parallel sense to both kinds of stimulation. During and after tetanisation the retinal excitability to light is increased. The results of these experiments will be published shortly.

(9) HERING'S THEORY OF COLOUR VISION (p. 18).

Hering first promulgated his celebrated theory in the sixth of a series of communications to the Vienna Academy of Sciences in the years 1872 to 1874, collected and reprinted for the second time in 1878 under the title *Zur Lehre vom Lichtsinne*.

The paraphrases of Hering's theory current in English text-books are far less subtle and indefinite than the version of

Hering himself, who writes as follows in the introduction of a paper by Hillebrand (*Wiener Sitzungsberichte*, February, 1889, p. 73) :—

"The psycho-physical vision-stuff may accordingly be regarded as a mixture of three qualitatively different substances. Nevertheless, I signified long ago (*Zur Lehre vom Lichtsinne*, § 42) that I gave this form to the theory only for the sake of greater distinctness, and that I consider it to be fundamentally more correct to say that the psycho-physical vision-stuff is capable of qualitatively different kinds of Dissimilation and Assimilation, and that each of these innumerably different kinds of D. and A., assuming three principal kinds of D. and A., can be conceived as broken up into three components, each of which corresponds to one of these three principal kinds of D. and A. It is, no doubt, more intelligible to most people to say that each visual sensation may be conceived as composed of given primary or elementary sensations, in given proportions, than to say that each visual sensation takes, in the pre-arranged three-dimensional variability of visual sensation, a given place in relation to three given sensation series ; and it is more intelligible to regard the vision-stuff as a mixture of three separate substances, each of which can be altered in two qualitatively opposite senses (D. > A. and A. > D.), than to say that the variability of state of vision-stuff is three-dimensional."

Helmholtz's theory, with which Hering's is generally quoted as being in flagrant opposition, is hardly more accurately reproduced in English text-books. In the second edition of his "Physiological Optics" (1889, p. 349), he assumes the hypothetical existence not merely of three sorts of retinal elements, but of three kinds of photo-chemically changeable substances, and of three kinds of cells in the cerebral cortex.

On a hypothesis of antagonistic colours of so meta-chemical a character as Hering's, positive results of experiments of the character described in the text might hardly be expected.

Previous experiments of the kind have been published by Dewar and McKendrick, who observed a different order of efficacy to that given in the text, viz :—red = 10, yellow = 10, green = 8, and blue = 4. Subsequently, however, they give the relative efficacy of colours as being governed by luminosity.

R. Dubois (*La Pholade Dactyle*, Paris, 1892) tested the efficacy of different colours upon the mechanical response of the integuments of *Pholas dactylus* with the following result :—red = 3, yellow = 13, green = 10, blue = 8. These numbers represent amplitude of reflex contraction of an integument excited by spectral colours. With coloured glasses the results were:—red = 3, yellow = 13, green = 10, blue = 8. With the same set of glasses—which Professor Dubois was good enough to send to me—I obtain electro-motive responses of the frog's retina as quoted in the text, viz.:—red = 4, yellow = 16, green = 12, blue = 8.

The researches of Dubois on the integument of *Pholas* are of great interest as regards the general physiology of luminous excitation, but are not yet sufficiently appreciated. There is a close structural and functional analogy between the retina and the integument of *Pholas*. Both respond to light—the former by an act of vision and by an electro-motive change, the latter by a reflex mechanical movement and an electro-motive change. The physiological histology of the sensitive surface is as follows:—An external layer of pigment-cells is connected with a superficial layer of muscular fibres that contract in response to luminous stimuli; this initial direct contraction mechanically stimulates subjacent nerve-cells, and is followed, after a short interval of time, by a reflex contraction of the entire longitudinal musculature of the syphon. Histologically, the dermic element excitable by light is composed of (1) a pigment-cell, (2) a contractile fibre, and (3) a nerve-cell. Physiologically, the stimulus of light arouses a dermic phosphene, of the nature of a tactile phenomenon, *i.e.*, light provokes chemical change in a pigment-cell, which in turn provokes movement of a contractile fibre, which in its turn mechanically excites a nerve-cell. This series of events at the periphery constitutes the physiological stimulus of which a reflex contraction of the syphon is the final consequence, just as a reflex movement of self-defence or flight is the final consequence of the retinal changes aroused by retinal images higher in the animal scale.

(10) HERING'S POSITIVE AFTER-EFFECT (p. 20).

A full description was first given of the after-effect of nerve-excitation and of its possible significance by Hering in 1884 (*Wiener Sitzungsberichte*, 1884, p. 137). The point was further investigated in Hering's laboratory by Head (*Pflüger's Archiv.*, vol. xl., p. 207, 1887).

(11) THREE STAGES OF NERVE-RESPONSE (p. 20).

The three stages into which I found it necessary to distinguish the response of isolated nerve, and the possible significance of the phenomena observed in each stage, are fully discussed in the Croonian Lecture for 1896 (*Phil. Trans. R.S.*, 1897, pp. 23 and 62).

(12) RAPIDITY OF NERVE-POLARISATION (p. 20).

Hermann pointed out in 1888 (*Pflüger's Archiv.*, vol. xlii., p. 1, 1888) that nerve, unlike muscle, exhibits no difference of resistance, whether the test-current be a constant or an induced current. Nerve is eminently polarisable (Herman's well-known theory of electrotonus rests upon this basis), but its polarisation and depolarisation take place with such extreme rapidity that the polarisation counter-current has time to develop even during the passage of an induction current.

Following up this point I found that the apparent resistance of normal nerve is higher to the comparatively "long" induced current at make than to the comparatively "short" induced current at break. Also that the apparent resistance of nerve to any current is diminished by diminution of polarisation counter-current, when the nerve-matter has been "immobilised" by chloroform (*Proc. Physiol. Soc.*, November, 1898).

(13) VERATRINE AND PROTOVERATRINE (p. 21).

The action of *veratrine* upon muscle was first described in 1862 by Harless (*Ztschr. f. rat. Med.*, iv., p. 97, 1862), and further studied by v. Bezold and Hirt (*Unters. a. d. physiol. Lab.*, Würzburg, 1867), J. L. Prevost (*Gazette médicale de Paris*, 1867), Fick and Boehm (*Arb. a. d. physiol. Lab.*, Würzburg, 1873), and many others.

Protoveratrine was identified and separated in 1890 by Salzberger, and its properties investigated by Watts Eden in the Pharmacological Institute of Leipsig, under the direction of Professor Boehm. W. Eden observed that protoveratrine, although poisonous to muscle, does not cause the prolongation of contraction characteristic of veratrine. The protoveratrine with which I made the experiments alluded to in the text, was kindly given to me for the purpose by Professor Boehm. I have described the results somewhat more fully in the jubilee volume of the *Société de Biologie*, Paris, 1899, p. 347.

SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD.

BY J. S. RISIEN RUSSELL, M.D., F.R.C.P.
Assistant Physician to the National Hospital for the Paralysed and Epileptic, Queen's Square, London.

F. E. BATTEN, M.D., M.R.C.P.
Pathologist to the Hospital;

AND

JAMES COLLIER, M.D., M.R.C.P.
Registrar to the Hospital.

INTRODUCTION.

MUCH as we feel the need of some other name under which to describe the affection, seven cases of which we are about to record, most of the papers that have appeared on the subject have borne the above or some similar title, so that to introduce a new name for the affection now would probably lead to confusion, however much it might serve to obtain for our own cases recognition that they are examples of a distinct morbid entity.

By combined degeneration of the spinal cord is meant an affection in which tracts of different function are concomitantly affected. It is, therefore, obvious that under such a title might legitimately be included a variety of different affections, each of which is characterised by the concomitant implication of tracts of different function. Examples of such affections are to be found in the "Ataxic Paraplegia" of Gowers, if there be such an affection distinct from the class of case with which we are more immediately concerned in our present paper; "Friedreich's Ataxy," "Cerebellar Heredo-Ataxy," such cases of "General

Paralysis of the Insane" as present degeneration in the posterior columns of the cord in conjunction with similar change in the lateral columns, and the like.

It therefore follows that there is need for a name that would serve to distinguish the class of case we are about to describe, from the affections that have just been enumerated, for it possesses a very definite clinical picture, not as a rule difficult of recognition, and a morbid anatomy which is as characteristic as that of tabes or any other disease of the spinal cord, with as distinctive a morbid picture as that possessed by the disease just mentioned. A name other than "Combined Degeneration," would undoubtedly do much to establish the affection as a separate and distinct morbid entity, would facilitate its study, and free it from the entanglements by which it is at present hampered, in consequence of the fact that so many different diseases of the spinal cord are characterised by combined degeneration of tracts of different function. We however, feel, that at present we shall probably be serving a more useful purpose by retaining the term "Combined Degeneration," and must trust to the "Subacute" as being sufficient to exclude most other forms of combined degenerations of the spinal cord, such as are likely to be confused with the affection now under consideration.

Its present name is, however, not the only entanglement from which it would be well to free the malady. The cases that were first recorded, and which led to the recognition of this disease as a distinct morbid entity, were described by Lichtheim as instances of cord changes associated with anæmia. Leichtenstern, the records of whose cases were next to appear, described the affection as "Progressive pernicious Anæmia in Tabetic Patients." In this way it has come about that the affection has become intimately bound up with anæmia, which has been variously described as "profound," "pernicious," "grave," "fatal," and so on. As a consequence of this, two totally distinct conditions have been confused, and in the literature that has grown up around the publications of Lichtheim and Leichtenstern we find cases of each recorded in a manner that suggests that the authors regard the affections as belonging to the same category, or, indeed, as if they are identical. Anæmia, in its relation to the subacute combined degeneration of the spinal cord, has to be considered from three points of view, in so far as the publications on the subject are concerned. There are the cases of subacute combined degeneration of the spinal cord with which we have to deal more directly in this paper, in some of which cases anæmia is a feature in the symptomatology; secondly, cases of anæmia in which certain symptoms arise which point to some disturbance of nerve function and in which certain changes are found in the spinal cord after death; and, lastly, cases of severe anæmia in which there have been no clinical phenomena pointing to disturbance of nerve function, but in which, nevertheless, histological examinations have revealed certain definite morbid changes in the spinal cord.

Cases of the first group are readily recognised clinically in consequence of the very definite symptomatology which they present, the phenomena pointing to serious structural defects in the nervous system; and the morbid changes found on necropsy serve to distinguish them from any other affection of the nervous system. In some of the cases anæmia is a striking feature in the symptomatology, while in others, if present at all, it is slight and unobtrusive.

The second class comprises a group of cases in which vague symptoms of a more or less indefinite character arise in the course of severe anæmia, which may or may not be characterised by the features which are supposed to be diagnostic of the so-called pernicious variety. The majority of the symptoms indicating implication of the nervous system point to interference of function consequent on molecular changes in the nerve elements rather than to gross structural changes in these parts. Histological examination, nevertheless, reveals gross changes in some such cases, and while these cannot be said to be identical with the changes found in the subacute combined degenerations, there is sufficient to make it impossible to deny that the changes found in these cases may represent an earlier stage of the affection which, when fully developed, presents so characteristic a morbid picture as that which we propose to lay before our readers.

The third group is composed of cases in which, though structural changes are found in the spinal cord on necropsy, there have been no symptoms during life which have pointed to affection of the nervous system. Nonne, Minnich, Burr and others have devoted attention to such cases, and all that can be said in this connection is that although they prove that structural changes may occur in the spinal cord in cases of anæmia, they do not admit of the interpretation that these defects are the earliest changes the full development of which are seen in the subacute combined degenerations, on examples of which our present paper is based.

All the cases like our own that have been published from the National Hospital for the Paralysed and Epileptic belong to the first category, and in all of them there has been the characteristic clinical picture supported by the equally typical morbid appearances found after death.

The first paper from this source was by the late Dr. Bowman and dealt with a single case; a paper by Dr. James Taylor dealt with two cases, and one by one of us (J. S. R. R.) was based on three such cases.

We are indebted to Dr. Hughlings Jackson, Dr. Buzzard, Dr. Bastian, Sir William Gowers and Dr. Ferrier for permission to publish the following cases, which were under their care in the National Hospital, and we take this opportunity of thanking them for their kindness.

CLINICAL ASPECT.

The following account of the clinical features of this disease is based upon nine cases in the wards of the National Hospital during the last three years. A *post-mortem* examination was made in seven of the cases. In the remaining two the diagnosis, although not established by pathological investigation, appears certain. One of these patients died shortly after leaving the hospital, but there was no opportunity for examination, and the other still remains in the hospital.

Added to the detailed clinical and pathological account in the appendix are three other cases, two of which are at present in the National Hospital, and the diagnosis of an early stage of combined degeneration seems highly probable, and a third, probably of the same nature, in which recovery has taken place.

In the first of these series of cases (No. 1) which came under our observation the symptoms were peculiar and striking, and the correct diagnosis was not made during life. In the remaining cases the aspect and course of the disease were so similar to those of the first case that a definite diagnosis was made and was confirmed by subsequent *post-mortem* examination.

So far as we may argue from these nine cases the clinical picture of the disease except in its earliest stage is very definite, and presents features which distinguish it from other affections of the spinal cord. The course of the disease almost always tends to a fatal issue. The changes in the clinical features which occur in the course of the malady are striking, and may be divided into three stages, separated the one from the other by abrupt transitions and by a marked change in the symptom complex; this constituting perhaps one of the most striking clinical features of the affection.

The three stages of the disease indicated may be summarised as follows:—

(1) A stage of slight spastic paraplegia with slight ataxy and marked subjective sensations in the lower limbs.

(2) A stage of severe spastic paraplegia with marked anæsthesia of legs and trunk.

(3) A stage of complete flaccid paraplegia; absent knee-jerks; absolute anæsthesia; rapid wasting and loss of faradic excitability in the muscles of the paraplegic region; increase of superficial reflex excitability; absolute incontinence of both sphincters and œdema of the lower extremities and trunk.

Though an anæmic state has hitherto held an important place in the symptomatology of this disease, and by some authors has been placed in important causal relation with the spinal cord lesions, we have not included this symptom in the foregoing summary of important symptoms, for the reasons that some of the most typical cases presented no anæmia throughout the whole course of the disease; others presented anæmia only late in the disease, when great general emaciation came on; while in other cases anæmia was an obtrusive symptom from the first, and preceded the manifestation of nervous symptoms by many months.

Repeated examination of the blood in the anæmic cases failed to reveal the alterations found in pernicious anæmia. The changes found were such as occur in cases of secondary anæmia. As regards the causal relation of this disease with pernicious anæmia it may be pointed out that according to the recent opinions of the highest authorities on the subject,[1] a diagnosis of pernicious anæmia arrived at from the character of the blood elements alone is quite unjustifiable.

ETIOLOGY BASED UPON THE OBSERVATION OF SEVEN CASES.

Age.—The disease appears in the fourth and fifth decades of life. The average age of the patients was forty years, the youngest being thirty years old, and the eldest being forty-nine years old.

Sex.—Women seem to be rather more commonly affected than men. Four of the seven cases were females, and three were males.

Heredity.—A slight family history of nervous disease was present in two cases. A marked tubercular family history was present in four cases. Acute rheumatism in three cases, and a history of cancer in two.

OTHER FACTORS.

These patients had been, without exception, strong and healthy till a short time before the symptoms became manifest. Four of them had a definite history of syphilis, and in two only could this be excluded with comparative certainty. There had been alcoholic excess in three of the cases, and prolonged suppuration in three others (pyonephrosis, chronic cystitis, and chronic bronchitis). In two cases the symptoms first appeared after pregnancy. Two of the patients lived in adjoining houses in the same street. All the patients were in comfortable circumstances, and no connection could be traced between the disease and acute illness or emotional disturbances.

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[1] S. Coupland, "Pernicious Anæmia," Allbutt's "System of Medicine,' vol. v., p. 504.

The onset of the disease was in most cases slow and insidious, and could not be attributed to any immediate exciting cause. In the most acute cases, however, the symptoms came on rapidly, and were ushered in by headache, vomiting, pyrexia, and malaise. Where anæmia had preceded the appearance of nervous symptoms, faintness, languor, palpitation, and irregular pyrexia were the symptoms which brought the patient under the notice of the physician.

The earliest manifestations of implication of the nervous system were subjective sensations in the lower extremities; numbness, a feeling of stiffness, and sometimes tingling. These symptoms were often so slight that it was many months before the patient sought medical advice, but once having appeared they were constant, and showed no tendency to disappear. Soon after these sensory manifestations, signs of slight spasticity and ataxy developed; the legs were clumsy and felt stiff and cold, and there was generally some dragging of the feet in walking. There was at this period of the disease no involvement of the cranial nerves, no girdle sensation, and no sphincter trouble. The signs present at this time were simply an increase of the deep reflexes in the lower extremities, the extensor response in the plantar reflex, and very slight loss of sense of passive position in the lower extremities. Similar symptoms and signs appeared in the upper extremities, generally at a later date than in the lower limbs, but sometimes coincidently, and the clumsiness of the upper limbs was first noticed by the patients in the act of writing.

The clinical picture was one of slight ataxic-paraplegia, and this constituted the first stage of the disease.

Whether the course of the disease was rapid, as in Cases Nos. 2 and 6, where the duration of the illness was four and three months respectively, or chronic, as in Cases Nos. 5 and 9, this stage usually occupied from a half to three-quarters of the whole duration of the illness.

The transition from the first to the second stage was usually abrupt, and was marked by the loss of ability to stand or walk, and by considerable loss of sensibility, to all forms, in the legs and lower part of the trunk. In five of the cases the change occurred in the course of a single night, and the patients, having gone to bed able to walk fairly well, found themselves unable to stand on getting out of bed in the morning. The inability to stand and walk was owing to loss of sense of position, and not to any marked loss of motor power, for this was quite good in some cases. Throughout the second stage the power of movement, as a rule, steadily declined, but was not completely lost in any muscle until the third stage—that of flaccidity—was reached. There were, however, two cases in which there was no marked loss of power until the stage of flaccidity was reached, and one in which the legs became completely paralysed, though still spastic. The muscles were rigid, and exhibited no marked wasting, and their electrical excitability remained normal. The most characteristic sign of the second stage was the rapid development of anæsthesia. Sense of passive position was absolutely lost in the lower limbs, and much impaired in the hands, which usually presented tabetic athetosis. Other forms of sensibility were impaired equally and in an increasing degree. The anæsthesia of the skin was always of peripheral distribution at first, appearing over the feet and hands; but as it gradually extended upwards it became segmental in distribution, and its upper limit upon the trunk was always a segmental limit, sharply defined. The highest level to which the anæsthesia has reached in any of the cases has been the upper limit of the sixth cervical root area (plates i. and ii.). In its progress upwards it may be limited for a

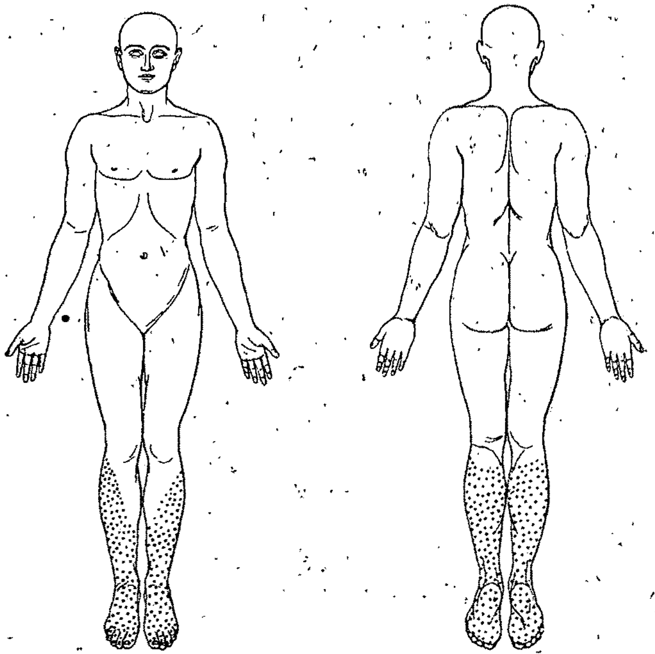

FIG. 1.

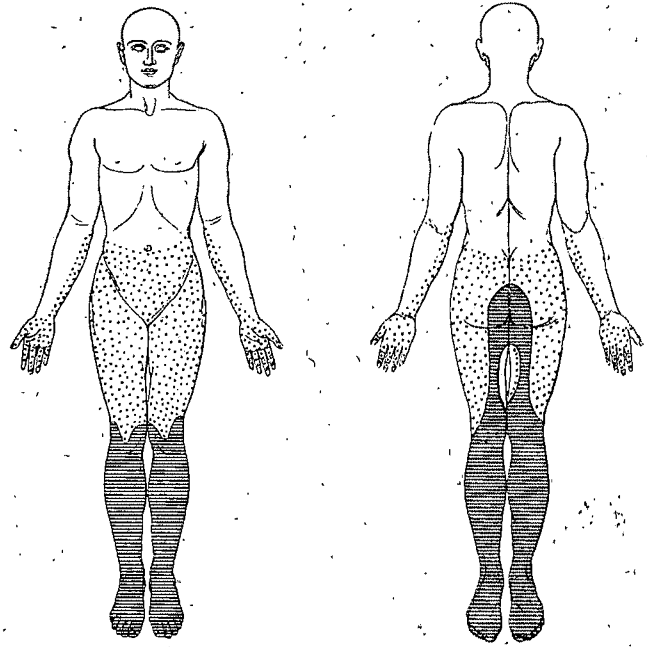

FIG. 2.

FIG. 1.—An early stage in the anæsthesia. Case No. 8.
FIG. 2.—Anæsthesia early in the flaccid stage. Case No. 4.

(The dotted areas represent partial, the lined areas complete, loss to all forms.)

PLATE II.

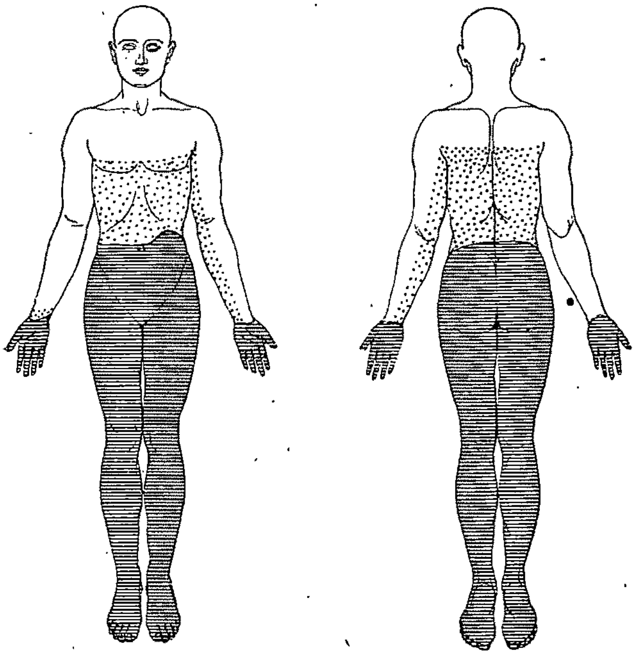

FIG. 1.

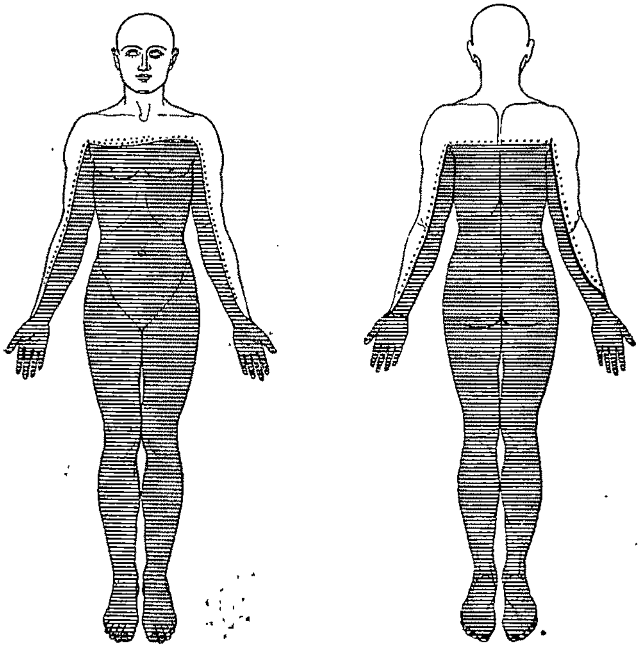

FIG. 2.

FIGS. 1 & 2.—Two late stages in the anæsthesia of Case No. 1.
(The dotted areas represent partial, the lined areas complete, loss to all forms.)

long time to a certain segmental level, and then suddenly encroach for several segments higher, and over the newly-involved area may show marked remissions and exacerbations in its progress to complete anæsthesia. Anæsthesia dolorosa and delay amounting to as much as fifteen seconds has been met with.

The lower lumbar and first sacral areas were always affected before the lower sacral and upper lumbar areas, and the lower cervical segments before the upper thoracic segments.

A girdle sensation in the lower thoracic region was common at this stage, and severe lightning pains in the lower extremities were frequent. A prominent feature of all the cases has been a severe constant dragging pain beneath the lower costal margin, always unilateral; in some cases on the right side and in others on the left.

Attacks of severe intercostal pain on one side were followed by herpes in two cases and in a third by a cutaneous hæmorrhage exactly limited to a nerve-root distribution (plate ix., fig. 1). Similar cutaneous hæmorrhages have been observed in cases of tabes dorsalis by Strauss[1] and others.

In this stage the mental faculties were not affected, and the special senses were found to be normal. Optic neuritis was not present, but in two of the anæmic cases multiple retinal hæmorrhages were found.

The cranial nerves were affected in some cases. Reflex iridoplegia was never present. Many of the cases presented slight nystagmus on extreme lateral deviation of the eyes. Weakness of the external rectus muscle with corresponding diplopia was present in two cases, and in one of them it was bilateral. Slight unilateral facial paresis was present in one case, and marked unilateral paresis and ataxy of the larynx, with alteration of voice, was present in one case.

The sphincters were in this stage often unaffected; in some cases there was slight incontinence, and in one case only complete incontinence. Considering the depth of the anæsthesia, this condition of the sphincters was remarkable, and contrasted very strongly with the absolute incontinence always present in the third stage.

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[1] Strauss. "Des ecchymoses tabétique à la suite des corses de douleurs fulgurantes," *Acad. de Neurologie*, 1881.

Trophic changes were not observed.

Both the superficial and deep reflexes were increased and the jaw-jerk and foot clonus were obtainable. A marked extensor plantar response was present in every case.

During this stage the general condition of nutrition may be good. In the patients with anæmia there were superadded the symptoms of that condition. Both the anæmic and the non-anæmic patients were subject to irregular elevations of temperature and symptoms of dyspepsia.

The length of this stage of the disease has varied in the different cases from three weeks to six months, but it was usually short, and occupied less than one-sixth of the whole time of illness. The average duration of this stage in the cases which have up to the present time proved fatal was five weeks.

The transition from the second stage—that of spastic paraplegia—to the third stage—that of flaccid paraplegia—occurred rapidly in the course of a few days, and was marked by the development of its following succession of symptoms in the lower extremities:—Absolute flaccid motor paralysis; absolute anæsthesia; complete incontinence of the sphincters; loss of the deep reflexes; rapid wasting of the muscles, with loss of faradic excitability; and œdema of the legs and trunk.

This change in the clinical picture occurred in most of the cases while they were under observation in hospital, and it was accompanied by a marked change in the general condition, malaise, drowsiness, anorexia, and general asthenia, becoming evident, and when anæmia was present, it became much increased. Pyrexia was always associated with the event. The accompanying temperature chart from Case 3 shows the behaviour of the temperature in all the cases in which the transition from the second to the third stage was observed.

The lower extremities, which before had been spastic

PLATE III.

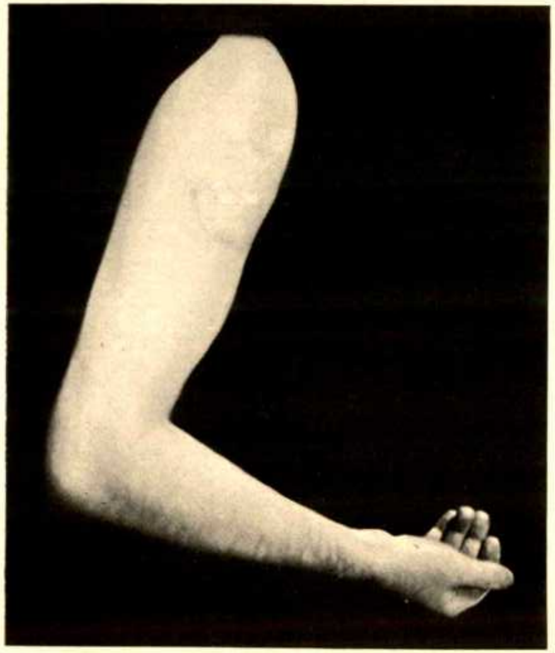


FIG. 1.—The right upper extremity of Case No. 7 when admitted.

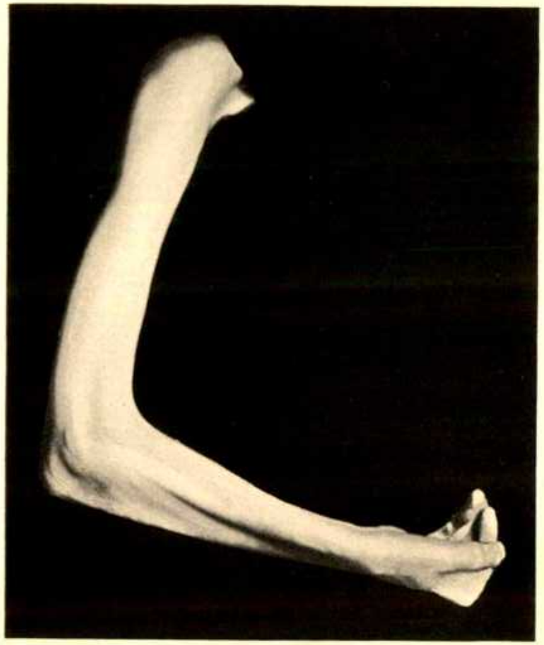
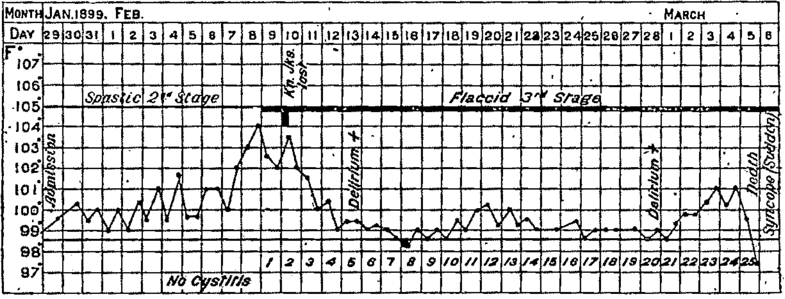


FIG. 2.—The same limb three days before death, showing the extreme muscular wasting.

with reflex spasms, epileptoid spasms, and increase of the deep reflexes, in the course of twenty-four hours became absolutely paralysed, the spasticity giving place to complete flaccidity with marked hypotonicity. The foot clonus was no longer obtainable, and the knee-jerks gradually becoming reduced to mere flickers upon reinforcement, were finally lost about four days after flaccidity had set in. Accompanying this flaccidity was the most striking alteration of the electric excitability, the faradic excitability rapidly falling almost to zero, and the galvanic excitability being much reduced, sometimes with and sometimes without a polar change. The diminution of faradic excitability was observed directly



Temperature Chart of Case 3.

the flaccid condition had set in. That the early change in the electric excitability was not due to the severe œdema of the subcutaneous tissues having insulated the deeper tissues was proved by the employment of sterilised needle electrodes plunged deep into the muscle, the condition of complete anæsthesia of the part allowing of this procedure. The muscles wasted rapidly. In the lower limbs and trunk the wasting was general, but in the upper extremities the wasting, which generally appeared later than in the lower extremities, affected first the intrinsic hand muscles and then the ulnar flexors, radial flexors, extensors of wrist, extensors of elbow, supinati, and fifth cervical group, in that order. This wasting continued throughout the third stage progressively affecting fresh muscles in an upward direction until, in the cases where the third stage was prolonged, there was extreme atrophy of all the observable muscles of the body, except those supplied by the cranial nerves (see plates 3 and 4).

The trunk muscles, with the onset of the third stage show complete paralysis below a segmental area, usually the ninth dorsal. Beevor's sign was well marked in all the cases (*i.e.*, the shifting upwards of the umbilicus in the attempt to sit up). Subsequently the upper abdominal and spinal muscles, the lower intercostals, and, in some cases, the diaphragm became completely paralysed.

With the exception of single instances in which paresis of the external recti, or of the face on one side, or of the larynx on one side, were met with, no paralysis of muscles supplied by the cranial nerves was noticed, nor were the neck muscles or the infrahyoid muscles affected.

The anæsthesia of the lower extremities and lower trunk rapidly became absolute, and the anæsthesia rose segment after segment; first relative, then slowly becoming absolute. In most cases the anæsthesia reached as high as the first dorsal segment before death, and in two cases it reached the sixth cervical segment (see plate ii.). Girdle pains, lightning pains, and paræsthesia were no longer complained of, but the heavy pain beneath the costal margin persisted to the end. With the onset of the flaccid stage the sphincters became in every case completely incontinent, but showed some reflex contraction to the usual tests. Cystitis occurred in several cases, but it was readily amenable to treatment, except in the cases with a long final stage. In these cases pyelonephrosis occurred. One of the most prominent symptoms following the change to the flaccid stage was the rapid appearance of much soft translucent œdema in the lower extremities and lumbar region. The œdema was much influenced by gravity, and could be readily removed from the feet by raising the legs. Becoming most marked on the fourth day of the flaccid stage, it showed remissions and exacerbations, and disappeared finally after about fourteen days.

PLATE IV.

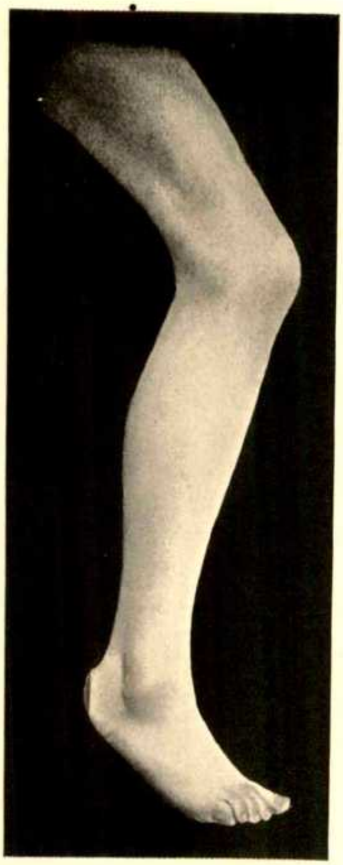


FIG. 1.—The right lower extremity of Case No. 7 when admitted.

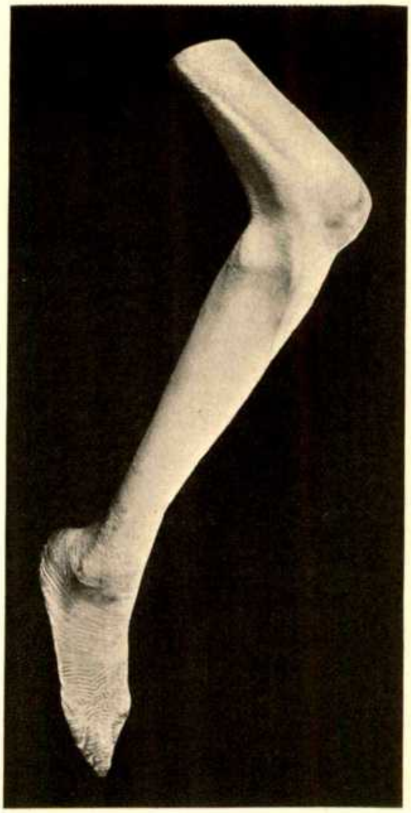


FIG. 2.—The same limb three days before death, showing the extreme muscular wasting.

Acute œdema of one arm, preceded by intense pain and lasting three hours, was observed twice in one case; but with this exception, no œdema was observed above the lumbar cushion. This symptom was present to a marked degree in every case. At this period signs of mental deterioration and disturbance appeared; drowsiness, childishness, nocturnal delirium, and varied delusions were common, and in one case there was prolonged maniacal delirium. Repeated convulsive attacks were noticed in three cases. The spasms were of a fine clonic nature, and affected the limbs only, and chiefly the periphery of the limbs. One of the patients (who only had two attacks) lost consciousness during the attacks, but in the other cases this did not occur. The convulsions were strikingly like those produced in some people by the administration of chloralose.

The condition of the cranial nerves did not alter during this stage. In some of the patients, towards the end of the illness, the pupils were small, with loss of the cocaine reaction (paralysis of cervical sympathetic).

The abdomen was invariably retracted.

Trophic changes in the skin, similar to those seen in neuritis, occurred in the extremities, and the patients, notwithstanding the utmost care, developed severe bedsores.

The deep reflexes were lost with the onset of the third stage, while the extensor response in the plantar reflex remained marked, and this combination of the signs of posterior and lateral tract involvement was found most valuable in the diagnosis of cases seen for the first time in the third stage of the disease. Case No. 8 came to the hospital at the beginning of the third stage, with incomplete flaccid paralysis of the legs, extreme ataxy, absent knee-jerks, and anæmia. There was a history of syphilis, and the case had been diagnosed as "tabes." The presence of the extensor response was not in accord with the diagnosis of tabes. This case was published in "An Investigation upon the Plantar Reflex," BRAIN, vol. lxxxvii., and it was then submitted that this alteration of the plantar reflex justified a diagnosis of postero-lateral sclerosis. Though there was no pathological verification in this case, the fact that she died three weeks later, with all the symptoms here described as typical of the third stage of combined degeneration, and that her own medical attendant subsequently furnished us with her earlier clinical history—one of spasticity and ataxy, foot clonus being present to within a few days of admission—places the value of this sign in this case beyond doubt.

A most remarkable fact, considering the wasting of the lower extremities, is that the general superficial reflex excitability of the skin of the lower extremities remains greatly exaggerated till quite late in the third stage.

The third stage, as a rule, lasted about six weeks, three weeks being the shortest period, and death occurred either from sudden syncope or respiratory failure. Two cases, however, lived five months and nine months respectively after the onset of the flaccid stage; but in these cases the onset of the flaccid stage was just as severe and the symptoms for the first few weeks quite similar to those in the more rapidly fatal cases. After reaching a condition in which death was hourly expected, these patients rallied a little and lingered a long time in a drowsy state of low vitality, with no fresh development of symptoms except progression of the muscular wasting and general emaciation. One of these patients would certainly have died in the eighth week of flaccidity of an attack of respiratory failure but for the use of artificial respiration and stimulants. The other case was aroused from a severe syncopal attack by powerful stimulants, without which it seemed probable that he would have died at a similar period. In the condition of mental and physical paralysis, profound anæmia, general emaciation, and sepsis in which these patients lingered for many weeks, it was difficult to conceive how life was maintained from day to day.

A remarkable feature of the cases was the absence of any improvement of the nervous symptoms under treatment. From the first appearance of the disease to the fatal event, the tendency was for the symptoms to increase, sometimes halting, sometimes progressing rapidly, but never showing any remission. Under treatment the general health and the anæmia improved markedly in some cases, but the nervous symptoms never.

All the patients, in whatever stage they came under observation, showed irregular pyrexia, and this entirely apart from any anæmic state; for the non-anæmic cases presented it markedly, and apart from the presence of any obvious cause, such as cystitis, bedsores, &c. The temperature was often subnormal, and the range of upward excursion did not exceed 102·5° F., and was usually about 100·5°F.; with the transition from the spastic to the flaccid stage there was always a marked increase in the pyrexia, lasting several days (see chart).

Though the passage from the first to the second stage was not actually observed in any case, it was ascertained with certainty in two of the cases from the private medical attendant of the patients that marked pyrexia had been present at that time.

In the clinical picture of this disease there remains to be discussed the anæmia, which may be considered under the following headings:—

(1) The anæmia preceded the appearance of the nervous symptoms, and was marked throughout Cases Nos. 3 and 4.

(2) Its date of appearance was coincident with that of the nerve symptoms, and increased with them. Case No. 7.

(3) It was only present at the end of a prolonged third stage, when emaciation became extreme. It was then profound. Case No. 1.

(4) There was no anæmia during the whole course of the illness. Cases 2 and 5.

(5) The blood was not examined. Case No. 6.

The characters of the blood were those of a secondary anæmia. The red blood-corpuscles were well shapen, except in Case No. 4, when the anæmia was most profound. A few small dark-coloured cells were generally present. Nucleated red blood-cells were only found in one case, and then in very small numbers. Gigantoblasts and microblasts were not found.

The number of leucocytes were increased both relatively to the red-cells and absolutely. The number of lymphocytes were relatively increased in all cases, and that of the coarse oxyphile-cells diminished. In three cases large oval-cells with reniform nuclei were found in small numbers.

The hæmoglobin was diminished in greater proportion than were the corpuscles. The diminution in number of corpuscles was most marked towards the end of the illness; for an instance in Case 4.

Two months before death—Hb. 56 per cent., R.B.C.'s 4,000,000.

Three days before death—Hb. 18 per cent., R.B.C.'s 800,000.

There was nothing in the blood of any of the cases in which it was examined to suggest "pernicious anæmia."

Neither the spleen nor lymph glands were palpably enlarged in any case.

Hæmorrhage was uncommon except from the bladder in connection with cystitis, when it was common. It was met with in the retina in two cases, and in the skin in one case, and in these cases it was not repeated. Thrombosis was not met with.

The usual symptoms of anæmia, air hunger, lassitude, syncopal attacks, &c., were marked.

In several cases the anæmia showed marked temporary improvement under treatment with iron and arsenic, but the improvement lasted only a short time.

The other organs of the body presented nothing worthy of special notice.

The clinical picture in three tableaux here set forth has been followed by all of these cases up to the present time fatal. The cases varied as regards the anæmia and the length of the illness. But if the slightness of the symptoms in those patients presenting a long first stage, and the conditions under which the third stage was prolonged in Cases 1 and 7, the regularity of the course of the disease as regards time is most striking.

Most of the patients have died within four months of losing ability to walk. The duration of the illness varying between three months and thirty months averages under nine months.

The following cases, which are included in the appendix, presented the clinical picture of the malady, but have not been verified.

Case No. 9, at the present time under the care of one of us (J. S. R. R.) at the National Hospital, we regard as an instance of the disease, and it suggests that in some cases the latter stages of the disease may be more chronic, especially the second stage, which in the other cases has been short, and in this case complete anæsthesia, complete incontinence and complete paralysis, with wasting of the muscles and diminution of faradic excitability are present, while the legs are very spastic and the knee-jerks increased with double foot clonus, that is, in the second stage, whereas, in the other cases, such symptoms only appeared with the onset of flaccidity and the loss of the deep reflexes.

Three other cases are recorded in the appendix. The first, No. 10, is submitted as a case of combined degeneration during a prolonged second stage, and the second, No. 11, as a case slowly passing from the second to the third stage. It is suggested that Case No. 12, in which recovery took place, was also of this nature—at all events, it could not be clinically distinguished.

DIAGNOSIS.

The differential diagnosis of combined degeneration, while it is simple in the later stages, presents great difficulty in the early stages. Since few of the cases in which the diagnosis has been verified after death were seen in the first stage, and since the clinical picture of that stage has been drawn almost entirely from the accounts of the patients and their friends (collected with every possible precaution to avoid error), and from the medical attendants of the patients at their own homes, and since no diagnosis of combined degeneration was made at the stage in any of these cases verified after death, we can do no more than point out the probable features that may lead to a correct diagnosis in the first stage.

The importance of early diagnosis is obvious from a point of view of prognosis, and it is possible that the disease may then be amenable to treatment.

The early clinical picture of combined degeneration, that of slight ataxy and spasticity, resembles closely that of the common paraplegic form of disseminated sclerosis in an early stage. Three of the cases here recorded were examined by competent authorities soon after their symptoms commenced and the diagnoses made by them, were :—

Case No. 3. Slight spastic paraplegia. Anæmia. ? cause.
Case No. 5. Early disseminated sclerosis.
Case No. 6. ? Early disseminated sclerosis.

In attempting to distinguish these two diseases, careful attention should be paid to the history. The age at which combined degeneration occurs is not the most common for the appearance of symptoms of disseminated sclerosis. The preponderance of subjective sensations in the legs, the absence of the functional manifestations, of exacerbations and remissions of the symptoms, of nystagmus, and of sphincter trouble which are so usual in disseminated sclerosis, and the presence of irregular pyrexia are probably of great importance in the early diagnosis of combined degenerations.

The presence of anæmia in an early case of spastic paraplegia should give rise to a suspicion, but the possibility of chlorosis, associated with disseminated sclerosis in young women, must be borne in mind. A symmetrical affection of all limbs, with slight ataxy and spasticity, preponderating in the legs, is a most important distinguishing symptom of combined degeneration.

In the second stage the diagnosis is more certain. The history of slight symptoms preceding a sudden complete and lasting helplessness of the legs; the preponderance at first of ataxy over loss of power; the rapidly-increasing anæsthesia, paresis, and spasticity; the severe lightning pains; the absence of sphincter trouble as a rule; the pyrexia and the ænemia, if present, serve to separate the disease from other forms of paraplegia.

In the third stage the diagnosis is easily made from the only diseases which present a symptomatology in any way resembling that of combined degenerations. These diseases are tabes dorsalis, acute myelitis, polyneuritis, and spinal tumour.

Most of the cases were sent to the hospital for the first time in this stage labelled "Tabes," on account of the flaccidity, anæsthesia, loss of deep reflexes, and complete incontinence. A history of spasticity changing rapidly to flaccidity, the completeness of paralysis and anæsthesia, the pyrexia, the œdema of the legs, the rapid muscular wasting and loss of faradic excitability, and that sure sign of involvement of the pyramidal system—Babinski's extensor response in the plantar reflex—at once excludes tabes dorsalis. Moreover, the Argyll-Robertson pupil was never present. In one case bilateral sympathetic paralysis had been described as "slight bilateral ptosis, marked myosis, and reflex iridoplegia." The sudden onset of complete paralysis and œdema resembles the onset of acute myelitis, but the preceding history will at once distinguish the two conditions.

A tumour pressing on the spinal cord, and giving rise in order to slight and severe spastic paraplegia, and finally to flaccid paraplegia, in some cases produces the picture most nearly approaching that of combined degenerations. The absence of severe root pains preceding the paralysis and the distribution of the physical signs in very unequal degree, in the upper and lower limbs, together with the absence of other distinctive signs of spinal tumour, should prevent an error in diagnosis.

The involvement of all the limbs, with flaccid paralysis, wasting, diminution of faradic excitability, anæsthesia, and loss of the deep reflexes are not unlike the symptoms of peripheral neuritis, but the resemblance is superficial only. The history of a preceding spastic state is incompatible with the diagnosis of polyneuritis. Total incontinence of the sphincters, paralysis of the trunk muscles, anæsthesia upon the trunk, following a root distribution, girdle sensations, and the presence of the extensor response in the plantar reflex are symptoms quite incompatible with a diagnosis of polyneuritis.

Prognosis.

So far as these cases are concerned the certain diagnosis of combined degeneration passes a short sentence upon the patient.

It may be, however, justifiable here to note that a patient of Dr. Ferrier's, at the National Hospital, suffered with a short illness associated with pyrexia, in which he suffered successively with slight ataxic paraplegia, severe ataxic paraplegia, and flaccid paraplegia, with wasting, œdema, and complete incontinence. After remaining flaccid for five days, he rallied from an apparently moribund state, and made a rapid recovery.

This patient is still under observation, and is at work. (Case No. 12.)

Treatment.

It has been already mentioned that under treatment with iron and arsenic the anæmia may improve greatly for a time.

No drugs have been found to influence the nervous symptoms in any way. Mercury, iron, iodide of potassium, arsenic, strychnine, quinine, salicylates, and various animal extracts have been given with no benefit.

MORBID ANATOMY.

The condition of the body at the time of death varied with the duration of the last stage of the disease. When this had been long, the limbs and especially the lower extremities were wasted, and in some cases this was extreme, and the legs had become contracted in the flexed position. In those cases in which the last stage of the disease was of shorter duration, the wasting was not so marked, and in these cases there was often a good deal of adipose tissue, not only over the trunk, but also over the extremities. Bedsores have always been present.

The brain, cerebellum, and pons in most cases appeared perfectly normal, but there was occasionally some wasting of the cortex, with slight thickening of the membranes and compensatory œdema. The vessels at the base of the brain appeared perfectly normal.

The spinal cord, apart from being slightly wasted (a condition, however, by no means always present) appeared perfectly normal, so far as its external aspect was concerned. There was, however, in one case slight opacity of the arachnoid membrane. On section of the cord, the gray appearance of the degenerated parts was at once obvious, and this became more marked after the cord had been hardened in Müller's fluid, when the sclerosed areas stood out of a lighter colour than the neighbouring healthy tissue.

The lungs have shown various degrees of œdema and patchy pneumonia, but otherwise have appeared normal.

The heart, both in regard to its valves and the condition of its walls, has appeared normal; in one case it was described as fatty. The pericardium has in all cases appeared normal.

The liver was generally enlarged to a slight degree, but showed no marked change; no free iron reaction has been obtained.

The spleen was found enlarged and soft, but the condition seemed to depend on the condition of the bladder and kidneys; for when these were normal the spleen did not manifest the above changes.

The kidneys often showed some change secondary to the condition of the bladder, either septic infarcts or pyonephrosis; in other cases they were either normal or showed slight granular change.

The bladder showed varying degrees of cystitis.

The bone marrow was examined in two cases from the femur, and in the first appeared red and almost diffluent, resembling the condition of the softened spleen; and this was a case in which the bladder appeared fairly healthy; in the second case it was of a more normal appearance, being pale and of the usual consistency. The muscles of the leg showed various degrees of atrophy, in most cases being flabby and very œdematous, but in others being simply wasted. The muscles of the upper extremity were much less affected than those of the lower.

PLATE V.

Series of sections from the medulla and spinal cord of Case No. 1.

The last stage of the disease in this case was of long duration, and consequently the amount of sclerosis is greater.

The sections have been stained by the Weigert-Pal method, and show the most marked change in the mid-dorsal region, where the whole of the periphery of the cord is affected, leaving the gray matter and a few medullated fibres in the immediate neighbourhood intact (figs. 4, 5, 6, 7). In the lowest of these, however, the whole of the periphery is not destroyed, a portion of the antero-lateral tract remaining intact (fig. 7).

In the lumbar region the disease tends to be limited to the posterior columns and the crossed pyramidal tracts, while in the sacral region, except for some slight affection of the crossed pyramidal tracts, the cord appears normal (figs. 8, 9, 10).

In the lower cervical region the destruction of the cord is still extensive, involving the periphery, but leaving a wider area of normal medullated fibres round the gray matter (fig. 4).

At the level of the first cervical segment (fig. 3) the most marked degeneration of the cord exists in the posterior columns and direct cerebellar tracts, but it is not limited to these.

In the medulla (figs. 1 and 2) the pyramids appear normal, but there is obvious degeneration in the region of the direct cerebellar tract and of the posterior column nuclei.

PLATE V.

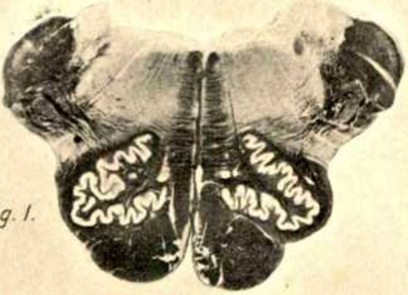


Fig. 1.

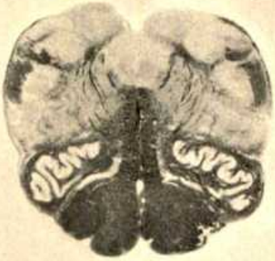


Fig. 2.

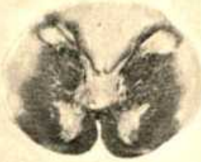


Fig. 3.

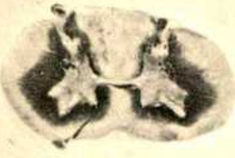


Fig. 4.

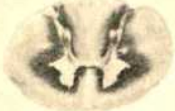


Fig. 5.

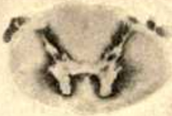


Fig. 6.

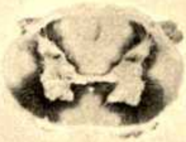


Fig. 7.

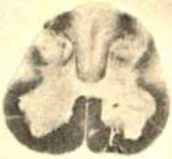


Fig. 8.

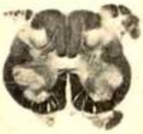


Fig. 9.

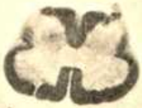


Fig. 10.

Case No. 1.

Microscopical Appearances.

The stress of the disease fell upon the mid-dorsal region of the cord, and therefore it will be convenient to commence with a description of the condition found in this region, and subsequently to pass to other portions of the cord. On examining a section of the cord taken from about the level of the sixth or seventh dorsal nerves stained by the Weigert-Pal method, it was at once apparent that there had been very marked destruction of the white matter of the cord all round the periphery, leaving the gray matter and a small area of white matter immediately surrounding it perfectly normal (see plate v., figs. 5 and 6, and plate vi., figs. 6 and 7); and it was apparent also that the destruction was not in any way limited to the long tracts of the cord, but affected the endogenous and exogenous fibres alike—in fact, all that was not in close proximity to the gray matter.

The posterior columns, which are generally most affected, may be completely sclerosed except for a small area in immediate contact with the middle third of the posterior horns.

If from this point in the mid-dorsal region the process was traced up the cord, it was found that the general destruction gradually became less, and, instead of affecting all tracts alike, tended to limit itself to the posterior columns (the columns of Goll being more affected than those of Burdach), the dorsal and ventral cerebellar tracts; and to the crossed pyramidal tracts (plate v., figs. 3 and 4, plate vi., fig. 3). But even in the cervical region, although these may be the most affected areas of the cord, yet the disease was by no means limited to them, for scattered degenerate areas were also present, a favourite situation for these being in the ventral region of the cord in the position occupied by the direct pyramidal tracts and the neighbouring ground bundles (plate v., fig. 4).

The destructive lesion was found as high as the upper portion of the medulla, but degenerate fibres could be seen by the Marchi method in the pyramidal tracts as high as the mid-region of the pons, and in the upper portion of the ventral cerebellar tract in the velum.

PLATE VI.

Series of sections from the medulla and spinal cord of Case No. 2.

The last stage of the disease in this case was comparatively short, lasting only about three weeks.

The sections have been stained by the Weigert-Pal method, and show the most marked degeneration in the mid-dorsal region. In this region (figs. 5, 6, 7, 8) there is degeneration both of the posterior and antero-lateral tracts, leaving the ventral portion of the cord unaffected except for a few scattered patches.

In the lumbar region (fig. 9) the degeneration is almost limited to the posterior columns and the crossed pyramidal tracts, while in the sacral region (fig. 10), except for some slight change in the crossed pyramidal tracts, the cord appears normal.

In the cervical region (figs. 3 and 4) there is marked degeneration in the neighbourhood of the crossed pyramidal tract and the posterior columns, leaving the ventral portion of the cord almost normal.

In the medulla (fig. 2) the pyramids appear normal, and the only degeneration visible by this method is that seen in the funiculus gracilis.

Although the degeneration has been described in certain tracts, it will be noticed that it is by no means limited to the strict margins of the tracts, and also that the degeneration occurs in patches, but that the margins of these never have the sharp edge that is commonly seen in disseminated sclerosis.

PLATE VI.

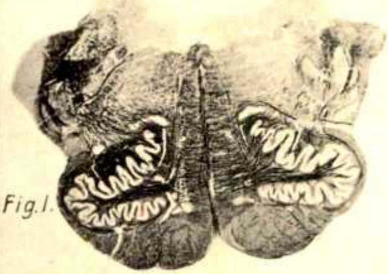


Fig. 1.

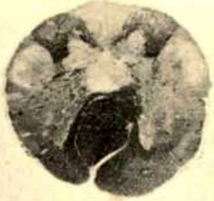


Fig. 2.

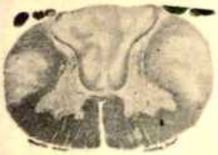


Fig. 3.

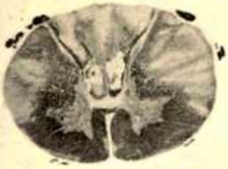


Fig. 4.

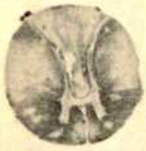


Fig. 5.

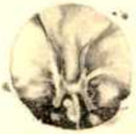


Fig. 6.

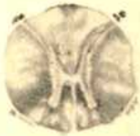


Fig. 7.

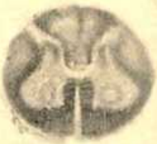


Fig. 9.

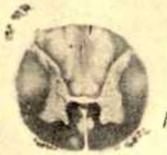


Fig. 8.

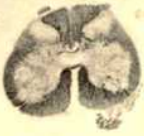


Fig. 10.

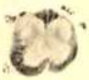


Fig. 11.

CASE No. 2.

The upper portion of the pons, the internal capsule, and the cortex of the brain appeared perfectly normal.

On passing to the condition of the cord below the mid-dorsal region, it was found that the diffuse destructive process steadily tended to diminish as the lumbar region was reached, and here it was usually found that the degeneration was limited to the crossed pyramidal tracts with some patchy destruction in the posterior columns, and possibly also in the ventral region of the cord (plate vi., fig. 8). In the sacral region the degeneration was almost entirely limited to the crossed pyramidal tracts, though in some instances patchy degeneration was present in the posterior columns also.

With regard to the condition as seen by the Marchi method, the same features as above described were observable, but it was found that the areas in which degenerate fibres could be seen were considerably wider than those which the Weigert-Pal method had indicated, and these recently degenerate fibres were present in largest numbers in that part of the affected area which bordered on the healthy white matter interposed between this and the vacuolated area to be described below. Degenerate fibres were also found scattered in the otherwise healthy white matter, in the vacuolated region, and to a much less extent or not at all in the sclerosed areas (plate vii.).

Lissauer's tract appeared, for the most part, normal on examination both by the Weigert-Pal and Marchi methods. In some cases it was rather pale as seen in sections prepared by the former method, but when compared with the normal tract the difference was not striking, and the absence of any recently degenerated fibres also seemed to support this view. Even in the mid-dorsal region, where the periphery of the cord was extensively affected, this tract, together with the apex of the posterior horn, escaped destruction.

There were obviously two distinct processes at work in relation to the alteration found in the spinal cords of these cases.

(1) A focal destructive lesion.

(2) A system lesion.

PLATE VII.

Series of sections from the medulla and spinal cord of Case No. 5 stained by the Marchi method. The sections have been drawn under an Edinger's projection apparatus.

In the medulla the most marked degeneration is seen in the direct cerebellar tracts and to a less extent in the pyramids (fig. 1).

In the cervical region (figs. 2, 3, 4) the areas of most marked degeneration appear to be the columns of Burdach, the pyramidal and direct cerebellar tracts, although the degeneration is by no means limited to these. The apparent absence of degeneration in the columns of Goll is accounted for by their complete sclerosis. The areas of degeneration are wider than those seen when similar sections are stained by the Weigert-Pal method.

In the dorsal region (figs. 5, 6, 7) the area of degeneration is wider, leaving only a small band without any degenerated fibres in the antero-lateral tracts.

In the lumbar and sacral regions (figs. 8 and 9) of the cord, degenerated fibres can be seen in the posterior columns, in the situation of the crossed pyramidal tracts, and in the ventral region of the cord.

PLATE VII.

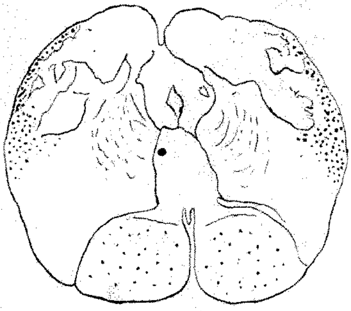


Fig. 1.

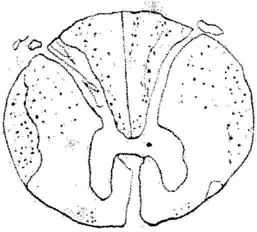


Fig. 2

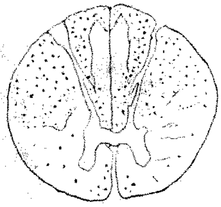


Fig. 5.

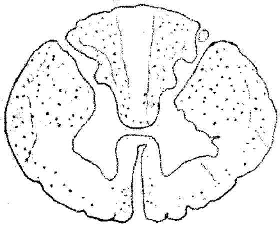


Fig. 3.

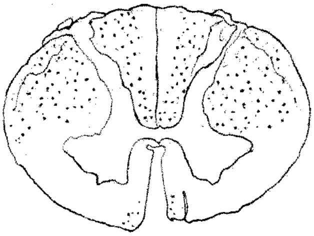


Fig. 4.

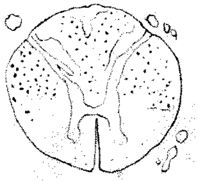


Fig. 6.

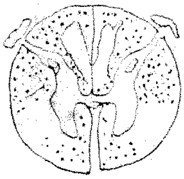


Fig. 7.

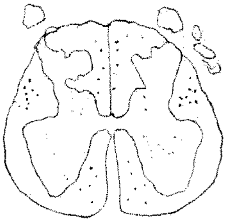


Fig 8.

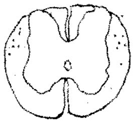
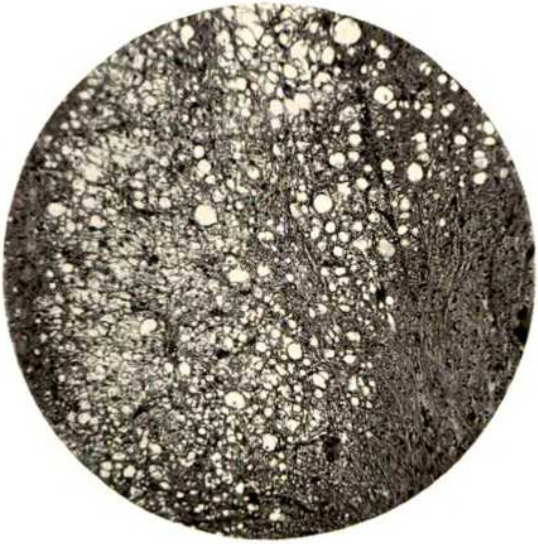


Fig. 9.

CASE No. 5.

PLATE VIII.



Transverse section of the spinal cord from the mid-dorsal region to show the vacuolated condition which occurs in these cases from the swelling of the medullated sheath and subsequent absorption of the products of degeneration.

The normal gray matter and some healthy fibres are seen to the left of the field, and some vessels with thickened walls can be seen in the vacuolated area. Magnified 43 diameters. The largest space seen in the centre of the field measures ·07 mm. in diameter. The normal medullated fibres in the same field measure rather less than ·01 mm.

while, on the other hand, similar changes were found in the posterior columns in the lumbar region.

The gray matter was practically normal. There were no degenerate areas present, nor were there any hæmorrhages, and, moreover, the vessels were neither thickened nor engorged.

The cells of the anterior horns and of Clarke's columns were for the most part normal; in certain sections of the cord, however, there were possibly rather fewer cells than normal, but those that remained were well stained. The nucleus and nucleolus were normal, as were the cell processes and the chromophilic granules, both as regards their arrangement and their staining; many of the cells were however extensively pigmented, this pigment being apparent not only by the Marchi method, but also by the Nissl method.

The anterior nerve-roots appeared normal both to the Marchi and Weigert-Pal methods, and this even in the dorsal region, where they lay in close contact with the degenerated areas within the cord.

The posterior nerve-roots and the posterior root ganglia appeared normal, although here again the cells contained a considerable amount of pigment. In one case, however—No. 7—in which a subcutaneous hæmorrhage had occurred in the area of skin supplied by the seventh left posterior root (plate ix., fig. 1), a cyst measuring 3 mm. in diameter and filled with clear fluid was found (plate viii., fig. 2). Many of the cells of this ganglion had undergone considerable atrophy, although others appeared perfectly normal. There was also an incision of the connective tissue between the cells. The vessels of the cord in the affected areas were engorged and their walls thickened, but there was no actual thrombosis. In the unaffected areas, however, the vessels were neither engorged nor thickened. An exceptional condition was, however, met with in one case in which the middle coat of the vessel appeared to have undergone a hyaline change. There was no obvious thickening of the membranes even over the areas in which the sclerosis of the cord was most marked.

With regard to the first, on examining the margin of the patches of degeneration, it was found that the earliest process that took place was swelling of the medullated sheaths, the axis-cylinders remaining apparently unaltered. The next step was that the swollen sheath underwent fatty degeneration, and this in turn became absorbed, and at the same time the axis cylinders disappeared, a space being thus formed, simply surrounded by the connective tissue of the cord. This space was often of considerable size from the fact that the individual spaces became fused into one another, and in those portions of the cord where the destruction had been most acute nothing was left but the connective tissue which formerly supported the now atrophied fibres forming the vacuolated areas above alluded to and figured in plate viii. In certain cases in which the condition had existed for a considerable time, or in those portions of the cord in which the disease was of longest standing, a considerable amount of fibrous tissue had become deposited in and about the loose meshwork, and a dense sclerosis of the cord had occurred in which neither spaces, medullated sheaths, nor axis cylinders could be seen.

As to the second process, viz., the system degeneration, it was found that the long tracts of the cord exhibited a degeneration similar to that which is found after transverse lesions of the cord, that is to say, there was degeneration of the medullated sheaths and axis cylinders and a gradual replacement by connective tissue giving rise to a definite sclerosis of the cord. The two processes merged into one another so closely that it was often impossible to say which was the focal lesion and which the system lesion, but as a general rule the farther from the mid-dorsal region the more easy it was to distinguish what appeared to be system degeneration from that due to focal changes, so that in the cervical region the system degeneration became more apparent in the afferent tracts, while in the lumbar region it was more evident in the efferent tracts, but it is not to be supposed that the change was limited to afferent or efferent tracts in either region, for extensive degeneration was found in the pyramidal tracts even as high up as the medulla,

PLATE IX.

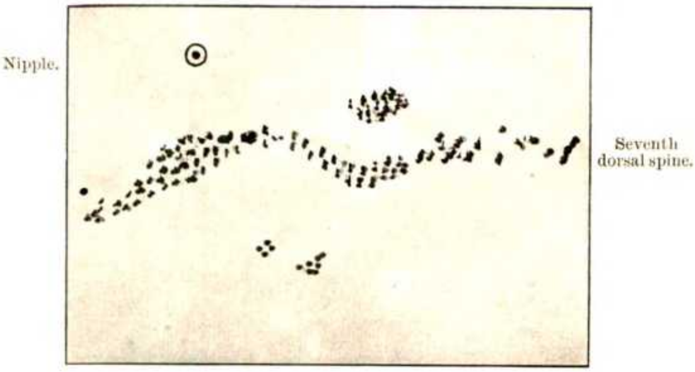


Fig. 1.

Subcutaneous hæmorrhage over chiefly the seventh left thoracic root area. The left limit of the figure is the middle line of the body in front, the right limit is the posterior mid-line. The seventh dorsal spine and nipple are indicated.

(*Traced from the body upon paper and reduced.*)

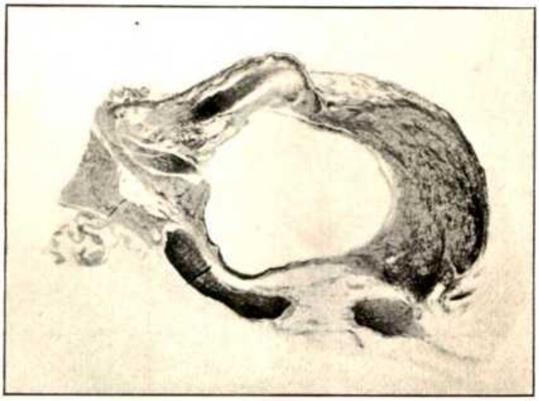


Fig. 2.

Section through the seventh left thoracic posterior root ganglion showing a cyst occupying the centre of the ganglion (case 7). The cyst measured 3 mm. by 4 mm. and was filled with a clear fluid. The walls of the cyst are composed of two coats, an outer of closely packed and an inner of loose connective tissue. Many of the cells of the ganglion are normal; altered and shrivelled cells are also present.—Magnified six diameters.

Nerves.—Various peripheral nerves have been examined, and in most of the cases they were found to be normal or showed only very slight changes, either by the Marchi or Weigert-Pal methods. In one case (No. 1), however, there was very considerable degeneration of the nerve-fibres —a change that not only occurred in the larger nerve-fibres, but which also involved the finer branches of the nerves within the muscles, and which appeared to affect not only the motor nerves but also those of sensory origin within the muscle-spindle. The degeneration of the nerves would seem to be a late manifestation of the disease, as this patient lived a long time after the disease was far advanced.

Muscles.—The condition of the muscle-fibres in these cases varied considerably, although they all showed atrophy; the degree to which this had taken place differed to a very great extent. In the most extreme case the fibres had become so reduced in size that they had lost their striation, and measured only ·004 mm. in diameter, and there was in this case a corresponding increase of the connective tissue (plate x., fig. 1). It was interesting to note that although the atrophy of the muscle-fibres had become so extreme, yet many of the finer nerve-fibres in the immediate neighbourhood were, to all appearances, perfectly normal. On the other hand, in the cases in which the atrophy was not so marked (and these form the greater proportion of the cases) it was found that the extent to which the muscle-fibres were reduced in size was such, that instead of measuring from ·06 to ·08 mm. in diameter, they measured on the average less than ·04 mm., and assumed a rounded instead of the polygonal shape commonly seen in muscle cut in transverse section after hardening (plate x., fig. 2). In a small number fat could be seen within the muscle-fibres; these were always fibres of small size, and usually measured from ·03 to ·02 mm. in diameter. This fatty degeneration of the fibres was rather the exception than the rule. There was no evidence of any inflammatory process, unless we accept the increase of connective tissue as having this significance; whereas, as above stated, this was sufficiently accounted for by the extreme atrophy which the muscle-fibres had undergone.

Muscle-spindles.—These organs appeared remarkably well preserved, especially when the atrophic condition of the muscle in which they lay was taken into account. The capsule and general appearance of the spindle was normal; the intrafusal muscle-fibres were of normal size, retained their striation, and only a few of them exhibited slight fatty degeneration. With regard to the nerves passing to the muscle-spindle, many appeared normal, and all those examined contained at least one normal fibre; when, however, we consider the large number of nerve-fibres which are normally present in the muscle-spindle, it seemed probable that there had been a certain amount of atrophy of the nerve-fibres even within the muscle-spindle.

The muscle-fibres of the diaphragm appeared normal.

The heart muscle appeared fairly normal; there was no fatty degeneration, but there was brown pigmentation of the fibres, extending from either pole of the nucleus of the fibre; the muscle-fibres did not appear much atrophied, and measured about ·02 mm.

The liver in the cases examined did not give the free iron reaction. There was some fat in the periphery of the lobules of the liver, but not in such amount as to be considered pathological.

The kidneys in those cases in which there had been infection from the bladder showed areas of small cell infiltration; in other cases they appeared normal, or showed slight fatty degeneration in the epithelium of the tubules.

PATHOLOGY.

Various views have been advanced as to the ætiology and pathology of the affection; but as these have been fully discussed in a former paper by one of us (J. S. R. R.), we do not propose to do more than epitomise the salient points brought out in that discussion. The spinal cord changes have been variously attributed by different writers to one or other of the following causes:—

PLATE X.

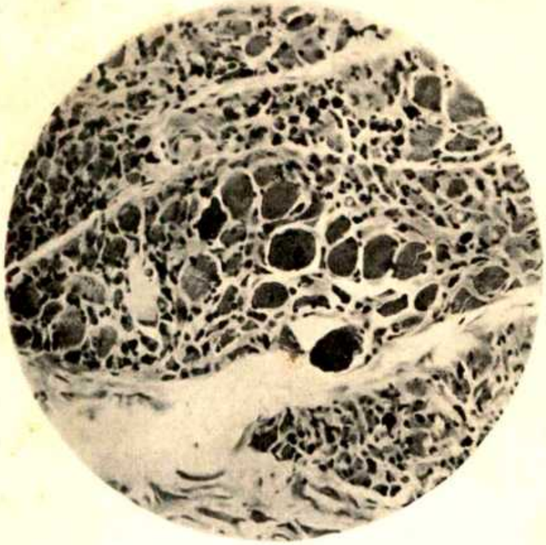


FIG. 1.—Transverse section from the vastus internus muscle of case No. 1, showing the extreme degree to which atrophy may take place. A portion of the muscle has been selected in which some comparatively large fibres remain, but the majority are atrophied to such a degree that they measure less than ·004 mm. The large muscle fibre in the centre of the field measures ·03 mm., *i.e.*, about one-half the diameter of a normal fibre.

There is a very considerable increase in the nuclei between the muscle fibres, but not more than can be accounted for by the fact that the normal connective tissue nuclei are approximated owing to the atrophy of the muscle fibres. Magnified 160 diameters.

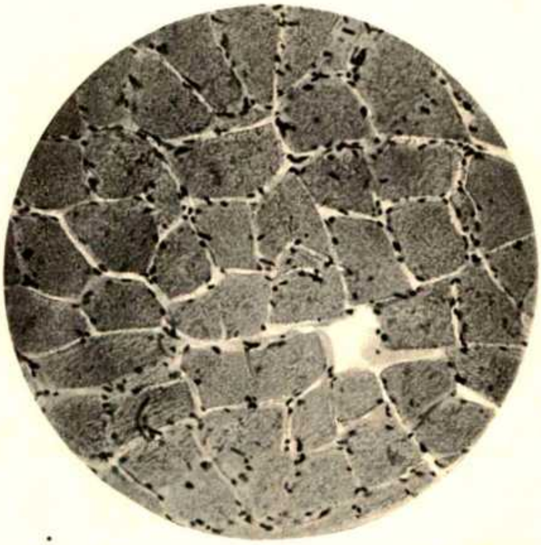


FIG. 2.—Transverse section from a normal vastus internus muscle for comparison with the above. The normal muscle fibres measure about ·06 mm. in diameter. Magnified 160 diameters.

(1) The anæmia frequently found in association with the spinal cord symptoms in these cases.

(2) Multiple hæmorrhages in the spinal cord occurring in association with the anæmia.

(3) Thickening of the walls of the blood-vessels, the vascular change being primary and that in the nerve elements secondary in origin.

(4) An acute myelitis occurring in the earlier stages of the disease, or a disseminated myelitis having a predilection for certain tracts of the spinal cord.

(5) The affection of the white matter secondary to a primary change in the gray matter of the cord.

(6) A toxic agent, which is jointly responsible for the changes in the spinal cord and for the anæmia in those cases in which this symptom is present.

The existence of so many different views on this question must, in part at any rate, be due to the opinions of writers being based on the particular conditions found in the cases which have come under their individual observation, and in greater part probably owing to the confusion that has already been alluded to, and in consequence of which cord changes occurring in the course of severe anæmia have been regarded as identical with the subacute combined degeneration of the cord in which anæmia may be a prominent symptom. A study of our own cases, in conjunction with all the recorded cases that strictly come within the same category does not, it appears to us, admit of such diversity of opinion.

The first point to be considered is what justification there is for regarding the cord changes as due to anæmia; but the objections to this hypothesis are so strong that we do not propose to devote much space to its discussion. Though a marked feature in many of the cases of the disease under consideration, anæmia has not been present, at any rate, to any notable degree in some, while in others in which it has been a prominent feature, the anæmia has not become obvious until some time after the spinal cord affection has manifested its presence by such clinical phenomena as we know indicate disturbance of this part of the central nervous system. Moreover, although cases of profound anæmia commonly occur, and although a large number of such cases which present the features of the pernicious and other varieties of anæmia have been examined by competent observers, in none of them have there been either clinically or after death the phenomena which characterise the class of case whose pathology we are now considering. Morbid changes have been found in the spinal cord in some cases of fatal anæmia, but in none of them have the changes been in any way comparable to those so characteristic of the group of cases of sub-acute combined degeneration. While dissenting from the view of those who hold that anæmia is responsible for the morbid changes present in the cases of combined degenerations, we are, nevertheless, prepared to admit the possibility that anæmia may play a part in reducing the resistive powers of the nerve elements, thus rendering them less able to withstand the baneful influence of toxins, a property which anæmia may be supposed to share with other debilitating influences and cachectic states. Thus it may happen that anæmia or other impoverished states of the system, themselves dependent on the action of some toxin, may in their turn render the nerve elements more susceptible to the action of the same, or, it may be, some other poison.

The view which supposes the degenerative changes in the various affected tracts of the cord to be due to small hæmorrhages is equally untenable, for no hæmorrhages were present in any of the cases included in our present series, nor could the slightest traces of former extravasations be detected. Even when hæmorrhages have been described as present, they have been too few, too small, and too scattered to possibly account for degenerations affecting tracts symmetrically and in their entirety throughout so large a part of the spinal cord, and producing so profound an alteration as to result in the complete degeneration of certain of them in parts of their course. Moreover, did larger hæmorrhages occur at certain points in the cord so as to interrupt the greater parts of the same tracts on both sides, we should find some evidence of ascending degenerations of certain tracts above such lesions with their escape, at any rate in part, below them, and of descending degenerations of other tracts below such hæmorrhages with partial or complete escape of the same tracts above them. Not only have no such hæmorrhages ever been met with, but the distribution of the degenerations in the cord quite precludes such a possibility. It is only necessary to remember that in most of these cases the degeneration both in the posterior and lateral columns is most pronounced in the mid-thoracic region of the cord, and that it diminishes in degree and extent in both pairs of tracts as we pass towards the cephalic and caudal extremities respectively.

The hypothesis which, while not regarding the degenerations in the cord as secondary to hæmorrhages, nevertheless assumes that they are of vascular origin in the sense that the degeneration commences in the immediate vicinity of vessels with altered walls, owes its origin to the observations of Nonne and Minnich, who both found areas of degeneration surrounding vessels with altered walls, but who were not dealing with the class of case whose pathology we are now discussing, but with cases of anæmia in which patches of degeneration were met with in the spinal cord. We have found nothing in the appearances of the morbid changes in the cords of our cases to justify the belief that the affection is vascular in origin in the sense that alterations occur primarily in the walls of the blood-vessels, and that the changes in the nerve elements are secondarily induced. That the topographical distribution of the degeneration of the white matter of the cord depends on the vascular distribution, however, there seems to be little question. This will be obvious if it be borne in mind that the blood supply of a given transverse area of the cord is mainly derived from two sources, the anterior median arteries in the anterior median fissure and the peripheral arteries derived from the vessels of the pia mater. The former supply the gray matter of the anterior horns and the white matter bordering on them, and the neck of the posterior horns, including Clarke's columns, while the latter supply nearly the whole of the rest of the white matter of the cord. The distribution of the affection in the white matter of the cord in these cases of combined degeneration is precisely that of these peripheral vessels. Why there should be the escape of the area of supply of the anterior median arteries is not clear, but this much seems certain, viz., that the affection of regions supplied by the peripheral vessels does not depend on pachymeningitis in these cases, for no such change has been found in any of our present series. This admission that the morbid condition owes its topographical distribution to the vascular supply must not be interpreted as meaning that we are of opinion that the degenerations of the spinal cord are vascular in the sense that they depend on changes in the vessel walls, whose impermeability leads to impoverishment of the nerve elements. That such thickening of vessels occurs, and that when it occurs it cannot fail to affect the nutrition of the parts supplied by such vessels is admitted; but that this is the primary cause of the degeneration of the nerve element is far from our belief. We regard such changes in the vessel walls as have been found as depending on the same cause as the parenchymatous degeneration of the nerve elements, or as resulting from irritative disturbance consequent on the degenerative changes in these; and that the only part played by the vessels in the initiation of the morbid changes in the nerve elements is that of bringing the toxic material to them.

The question of the vascular supply of the cord and its influence on the topographical distribution of the morbid changes is, however, of interest from another point of view. It is tempting to assume that the fact that the most extensive changes are met with in the mid-thoracic cord is due to the fact that this portion of the cord is less well supplied with blood than any other part, a view that would appear to receive some support from the fact that it is in this region that we most commonly meet with transverse softening, presumably due to vascular thrombosis and unfortunately and erroneously designated transverse "myelitis." On searching for anatomical evidence, however, in support of the view that the mid-thoracic region of the spinal cord is least well supplied with blood, we can find little to justify the assumption, most of the evidence from this standpoint indicating rather that it is the lowest part of the thoracic cord and the lumbo-sacral region that is least well supplied with blood, both because this part of the cord is farthest from the origin of the anterior and posterior spinal arteries which are derived from the vertebrals in their course within the cranial cavity, and because the reinforcing arteries which reach the spinal cord by way of the nerve-roots have both a longer and a more vertical course from below up to this part of the cord, in addition to which of all the reinforcing arteries these are farthest away from the heart. Some observations conducted by Dr. Carrington, and referred to by the late Dr. Moxon in one of his suggestive Croonian Lectures (*Lancet*, 1881, i., p. 530), are worthy of attention in this connection. Injections were made into the femoral arteries in seven dead bodies, and in spite of its being *a priori* more probable that the vessels at the lower end of the spinal cord would be better injected than those at the upper end, the reverse obtained. In all the subjects the spinal arteries filled from above down, the injection either ceasing at the lower end of the cord or above that part, and while it was obviously reinforced by vessels which entered along the nerves, in no case were the reinforcing vessels of the nerves of the cauda equina found injected.

Much as all this bears against the possibility that the part of the cord most affected in the combined degenerations is that least well supplied with blood, it has to be remembered that it is not in the region of supply of either the anterior or posterior spinal arteries, or of the reinforcing arteries that enter the spinal cord by the nerve-roots that the degenerations occur, but that the degeneration is in the area of supply of the pial vessels.

We have next to consider the view that the spinal cord affection in the sub-acute combined degenerations is the result of myelitis. The objection which has been advanced against considering the degenerations as the result of hæmorrhages, to the effect that parts of certain tracts should be affected above such lesions and should escape below, while others should be affected below and escape above, is equally applicable in the case of myelitis. Then, again, although we see all stages, including what appears to be the earliest of the changes in the spinal cord, we never meet with a round cell infiltration of the tissues so characteristic of changes of inflammatory origin.

The view that attributes the changes in the white columns of the cord to a primary affection of the gray matter appears to us to be erroneous in that in no small proportion of the total number of recorded cases, including all those of our present series, the gray matter has been found intact, while in a large number of cases in which changes have been found in the gray matter they have been slight and insignificant compared to the degeneration of the white matter, so that the latter could not possibly depend on the former changes. Moreover, there is a wonderful symmetry in the affection of the white matter, while changes in the gray matter when present are, as a rule, irregularly distributed. A further argument against this view is to be found in the fact that the parts of the white matter which chiefly escape are largely those the fibres of which are of endogenous origin.

There only remains for our consideration the view that a toxic agent is jointly responsible for the changes in the spinal cord and for the anæmia in those cases in which this symptom exists; and to this view we strongly incline. Although no poison has been determined in these cases, both the clinical picture and the morbid changes suggest that some toxin is responsible for the production of the disease. This toxic body (whatever may be its chemical nature) may reasonably be supposed to produce a parenchymatous degeneration by its action on the nerve elements of the spinal cord. Such a theory accords best with the changes found and with their distribution. The most reasonable explanation that can be offered as to why some parts of the cord are affected and others are not is that all parts of the central nervous system are not equally prone to be deleteriously affected by one and the same toxic agent, and that while certain parts are exceedingly easily damaged by one poison, others have a peculiar power of resistance to the action of such a toxin, while it may be that these very parts are much less able to resist the action of some other toxin which may have little or no effect on the parts so susceptible to a poison having different properties.

APPENDIX OF CLINICAL CASES AND PATHOLOGICAL RESULTS.

Case 1.—M. M., a stevedore, aged 27 years, was admitted into the National Hospital under the care of Dr. Bastian on October 27, 1897, complaining of numbness and loss of power in the legs and dysuria. He had always had the best of health previous to this illness. He denied venereal disease, and no fact was elicited suggesting that he had had syphilis. He had never taken excess of alcohol. He had suffered from a winter cough for many years.

Five months before admission he began to notice that his legs were numb and stiff, that he dragged his feet in walking, and caught his toes in the ground. A tight feeling round the lower chest troubled him greatly at times. A few weeks later he became unsteady when walking in the dark, and fell into his basin on several occasions when washing himself. He was treated at the London Hospital, where his condition was described as one of spastic paraplegia with ataxy and much anæsthesia of the legs. For three months before admission he had been losing his memory, and had become dull mentally.

Ten days before admission he became unable to stand or walk, and for the first time in his illness became unable to hold his urine. The legs which had been stiff till this time became quite flaccid. He had never had any shooting pains or "crises."

When admitted he was a powerfully built, ruddy faced man. He was not anæmic. Mental state dull and drowsy. Memory bad. Special senses normal. Pupils equal and reacted normally. Divergent strabismus due to weakness of the right internal rectus; otherwise the cranial nerves were normal. Erectores spinæ and respiratory muscles normal. Great weakness of the lower half of the abdominal muscles, the umbilicus shifting upwards an inch on the attempt to sit up. All the movements of the upper extremities were very weak and were accompanied by tremulous incoordinate movements. The intrinsic hand muscles were wasted, and he could not approximate the thumb and little finger of either hand. There was marked hypotonia of the upper extremities. The electrical reactions of the muscles were normal.

Table of all the Physical Signs and Symptoms that have occurred in the Cases 1-9.

	First Stage.	Second Stage.	Third Stage.
Mental symptoms	—	—	Puerility; Delusions; Mania; Coma
Convulsions	—	rare	occasionally present
Speech and articulation	—	—	—
Special senses	—	—	—
Cranial nerves	—	sometimes affected	—
Nystagmoid movements	—	present	present
Pupils	equal and react	equal and react	equal and react
Palsy of trunk muscles	—	spastic palsy	flaccid palsy
Palsy of diaphragm	—	—	sometimes present
Upper extremities :—			
Paralysis	? slight	slight or marked	spastic or flaccid
Wasting	—	sometimes present	marked
Ataxy	present	marked	severe
Lower extremities :—			
Paralysis	slight spastic	severe spastic	complete flaccid
Wasting	—	sometimes present	severe
Ataxy	present	severe	extreme
Subjective sensations	present	present	present
Shooting pains	—	present	present
Girdle sensation	—	present	often present
Pain beneath costal margin	—	—	present
Herpes	—	present	present
Anæsthesia	—	partial loss	complete loss
Sphincters	—	usually normal	incontinence
Superficial reflex excitability	+	+ +	+ +
Plantar reflexes	? extensor	extensor	extensor
Deep reflexes	increased	increased	lost
Pyrexia	present	present	present
Anæmia	present	present	present
Hæmorrhages	—	—	present

All movements of the lower extremities were performed feebly. The muscles were hypotonic, but were not wasted, and the electrical reactions were normal. When supported on either side he could just stand. The attempt to walk produced the most wildly incoordinate movements. There was complete loss of sensibility to all forms below the ninth dorsal root level and impairment to all forms as high as the fourth dorsal root level, and over both hands and the ulnar border of the left forearm. There was a marked girdle sensation immediately below the ensiform cartilage, and he complained of a constant heavy pain in the hepatic region. Reflex incontinence of urine with a considerable amount of residual urine. Severe cystitis. Cranium and spine normal.

Reflexes.—Wrist and elbow-jerks absent; knee-jerks only just obtained with double reinforcement; no foot clonus. Superficial reflex excitability of the lower limbs much increased. The plantar reflexes showed the extensor response. Some chronic bronchitis and emphysema. Temperature 101° F. No palpable enlargement of the spleen. The other organs were examined and found healthy.

A few days after admission the knee-jerks were lost and were never again obtained. The legs rapidly became completely paralysed. The muscles of the legs, forearms, and hands wasted rapidly, and their faradic excitability was lost early. Severe œdema of the legs and trunk appeared and lasted about a month, subsequently disappearing. He was twice seized with an attack of fine clonic spasm in all four extremities, without loss of consciousness. The anæsthesia became absolute everywhere below the sixth cervical root level. He became generally much emaciated, and died of asthenia on June 8, 1898. The blood examined two months before death showed hæmoglobin 25 per cent., R.B.C.'s 1,500,000 per cm. No nucleated red cells present.

Duration of illness—fifteen months; stage of slight ataxic paraplegia with anæsthesia—five months; stage of severe paraplegia with + knee-jerks—one month; stage of flaccid paralysis with absent knee-jerks, wasting, loss of faradic excitability, and œdema—nine months.

Post-mortem Examination.

The body was extremely wasted, the wasting being most marked about the lower extremities, which were fixed in a position of partial flexion at the hips and knee-joints. There were several bedsores, both healed and open. There was an abscess in the left groin. Brain and membranes were normal. Spinal cord in external appearance was natural, but on section showed distinct sclerosis of the posterior and lateral columns. Heart and pericardium were normal. Lungs showed some patchy pneumonia. Liver was natural. Spleen was enlarged and friable. Kidneys were both enlarged, and showed a condition of pyonephrosis. Bladder showed evidence of chronic cystitis.

In sections prepared by the Weigert-Pal method all that was obviously wrong with the medulla above the level of the posterior column nuclei was degeneration in both lateral regions in the area occupied by the ventral cerebellar tract. More caudally there was, in addition to the degeneration in this situation, marked degeneration of the fibres of the posterior column nuclei and of the restiform body to a much slighter extent. Nothing obviously abnormal could be determined in the pyramids. In the upper cervical region there was complete degeneration of the posterior columns, the parts bounding the gray matter alone escaping. There was also marginal degeneration affecting the direct cerebellar and posterior part of the afferent antero-lateral tract, encroaching slightly on the crossed pyramidal tracts. The ventral part of the cord was preserved, with the exception of a very slight symmetrical degeneration in a very limited area in the efferent antero-lateral tract area. Lower in the cervical region some more of the postero-external column was preserved, the degeneration being on the whole less intense in this tract than in the postero-internal. There was in addition marginal degeneration, which affected the whole of the periphery of the remaining parts of the cord, including the direct pyramidal down to the anterior commissure. The crossed pyramidal tracts were considerably encroached upon, while the degeneration was rather less marked in the position of the efferent antero-lateral tracts than elsewhere in the affected parts. The same topographical distribution of the degeneration obtained in the thoracic region, though the extent of the area affected was greater; a smaller unaffected boundary separated the gray matter from the degenerated parts in the lateral and ventral regions of the cord, so that the crossed pyramidal tracts, for instance, were wholly involved while the lateral limiting layer escaped. In the lumbar cord the degeneration was less extensive in distribution; a considerable area in the antero-lateral region escaped, and there was no marginal degeneration at this point. In the posterior columns the fibres of the efferent septo-marginal tracts were seen to be unaffected. In the lower lumbar and sacral regions the ventral portion of the cord was quite normal, the degeneration being limited to the crossed pyramidal tracts.

Sections prepared by the Marchi method confirmed what was shown by the Weigert-Pal method, and added the following information:—In the medulla, scattered recently degenerate fibres existed in both pyramids, and the areas of degeneration were more extensive than would be supposed from a study of the sections prepared by the other method alone. The same applies to the cord, for recently degenerate fibres were seen in areas which otherwise appeared normal. This method made it clear that in the affected parts three zones existed—(1) of advanced change, in which there was thick-set sclerosis, and little if any recent degeneration; (2) in which the bulk of the fibres was normal, but recently degenerate fibres were scattered throughout them; (3) an intermediate zone, in which the marked feature was the large clear spaces from which the products of degeneration had escaped. Thickened septa separated these spaces and scattered recently degenerate fibres, fewer than in the better preserved parts and more than in the sclerosed parts, lay among them.

The Nissl method revealed no abnormality in the cells of the gray matter of the cord, nor in those of the posterior root ganglia, nor could any change be determined in these parts by other methods of staining.

The nerve to the vastus internus muscle showed very considerable degeneration both by the Marchi and Weigert-Pal methods; by the Strœbe method many normal axis-cylinders could be seen, but it was noted that the medullated sheath of the nerve also tended to take the blue stain in an irregular manner, and a similar appearance was seen in the nerves of dogs in whom recent degeneration had been experimentally induced.

Muscles.—In the vastus internus there was extreme atrophy of the muscle-fibres, with a corresponding increase in the interstitial tissue between the fibres (plate v., fig. 1). There was also a considerable amount of fat within the individual muscle-fibres, and the transverse striation had disappeared from almost all, except a few of moderate size; but it is extraordinary to note how many apparently healthy well-medullated nerve-fibres lie in an area of muscle which is absolutely degenerate. Some of the atrophied muscle-fibres measured only ·004 mm., and even the largest measured only ·036 mm. The finer intermuscular nerve-fibres showed degeneration.

This case was examined also especially with regard to the muscle-spindle; it was found that the spindle, not only when teased out but also on transverse section, appeared normal, except for the fact that the nerves did not in every case stain well; the striation of the muscle-fibres within the spindle was well preserved, and apart from some fat within the fibres, they were normal. When stained by the Weigert-Pal method the nerve-bundles passing to the spindle stained badly, and comparatively few fibres were seen within the spindle; when, however, we consider the advanced degeneration of the muscle, the condition of the spindle was well preserved, although the nerve supplying it would seem to have undergone considerable degeneration.

Case 2.—J. S., a police constable, aged 36 years, was admitted into the National Hospital, under the care of Dr. Ferrier, on January 4, 1899, complaining of numbness and loss of power in all four limbs and loss of control over the sphincters.

His family history was unimportant. He had suffered with rheumatic fever and typhoid fever in childhood. He denied venereal disease. He had never indulged in excess of alcohol. He had always enjoyed good health, but had been much exposed to the weather.

The history of the illness was as follows:—On September 14, 1898, while at drill, he suddenly felt faint, and on reaching home vomited and had severe headache, which lasted three days. At the end of this time, on getting out of bed one morning, his ankles gave way under him, and from this time he suffered with a dull heavy pain in the loins and with a tight feeling round the stomach. The legs became numb and stiff, and he dragged them in walking. He was very ill generally, and frequently vomited.

In November, 1898, he rapidly lost power of standing, and suffered with severe shooting pains in the legs.

A month later the legs became completely flaccid, and he lost control over the sphincters. He suffered greatly with dyspnœa at this time.

When admitted he was a well-built healthy-looking man, with a flushed face and a distressed expression. He lay in bed breathing rapidly, and was unable to sit, stand, or walk. There was much soft œdema of the legs and trunk, and a large superficial sacral bedsore. The temperature ranged between 99° F. and 101° F.

His mental state was intelligent. He was delirious at night. The special senses, optic discs, and cranial nerves were normal. The pupils were equal and reacted normally.

The abdominal muscles, lower part of the erectores spinæ, and diaphragm were very weak, breathing being almost entirely thoracic.

The upper extremities were weak, but all movements could be performed against some resistance; no rigidity nor wasting. There was extreme incoordination and tabetic athetosis in both upper limbs.

The lower extremities were completely flaccid, and hypotonus was extreme. He could just move all the joints of the legs, but not against the least resistance. All the muscles of the limbs responded normally to both faradism and galvanism.

He complained of an intense heavy pain in the left hypochondriac region and of a broad girdle-sensation between the umbilicus and the ensiform process. Severe shooting pains in the legs. There was marked loss of sensibility to all forms below the twelfth dorsal root level, and generally ten seconds' delay in the perception of severe painful stimuli. There was complete loss of sense of passive movement in arms and legs. There was complete incontinence of sphincters, and there was cystitis.

Reflexes.—Wrist, elbow and knee-jerks absent; no foot clonus. Superficial reflex excitability of the lower limbs greatly increased. Plantar reflexes showed extensor responses.

Heart and lungs normal. Spleen not felt. No anæmia.

After admission the lower extremities rapidly became completely paralysed; the muscles wasted and lost their faradic excitability. The same event happened somewhat later in the hands and forearms. The diaphragm and lower intercostals became paralysed, and respiration became much embarrassed.

The anæsthesia gradually became complete, first over the sacral root areas and then step by step upwards till it reached the upper limit of the fourth dorsal root area.

The muscular wasting increased, and the galvanic excitability became much reduced. The knee-jerks were always absent. The superficial reflex excitability of the legs remained excessive. The extensor responses remained marked.

The patient died of respiratory failure twenty days after admission. Blood count two days before death: hæmoglobin 90 per cent.; red corpuscles 4,500,000 per c.mm.; no nucleated red cells.

Duration of symptoms—four months; stage of slight ataxic paraplegia—nine weeks; stage of severe palsy with rigidity—four weeks; stage of flaccidity, wasting, loss of faradic excitability, absent knee-jerks, and complete anæsthesia—three weeks.

Post-mortem Examination.

The body was poorly nourished, the wasting of the lower extremities being out of all proportion to that of the rest of the body; a bedsore was present over the sacrum. There was some patchy consolidation of the lungs. The spleen was enlarged, but the other organs of the body appeared healthy. The spinal cord, so far as its external surface was concerned, appeared to be healthy, but on section degeneration in the posterior and lateral columns was apparent.

Microscopical Examination.

Cortex.—The cells of the cerebral cortex and the tangential fibres appeared normal; no degeneration could be seen by the Marchi method. The cerebellum and pons appeared perfectly normal.

Medulla.—The upper portion of the medulla appeared perfectly normal both by the Marchi and Weigert-Pal methods. At the level of the posterior column nuclei there was by the Marchi method degeneration in the funiculus gracilis and cuneatus and in the direct cerebellar tracts, but only a few degenerate fibres could be seen in the pyramids. By the Weigert-Pal method degeneration could only be seen in the funiculus gracilis.

Spinal cord.—The brunt of the disease had fallen on the mid-dorsal region, and had affected the posterior columns and the region occupied by the crossed pyramidal tracts more than the ventral region of the cord, although there were numerous patches of degeneration even in this area. In the cervical region the degeneration was limited to the posterior columns, the crossed pyramidal and the direct cerebellar tracts, and had left the ventral portion of the cord even less affected than in the dorsal region. The degeneration was much more scattered and patchy than in some of the other cases, and did not affect the whole periphery of the cord in the mid-dorsal region to so marked an extent.

By the Marchi method there was considerable degeneration both in the regions above described and also around them. There was considerable vacuolation in the mid-dorsal region of the cord, but the recent degeneration, as shown by the Marchi method, was most marked in the long tracts of the cord.

By the Nissl method the cells of the anterior horn, although somewhat pigmented, appeared perfectly normal; the cells of Clarke's column also were normal.

By van Gieson's method there was considerable thickening of the walls of the vessels in those areas of the cord where the degeneration was most marked, while in the region of the cord where there was no change there was no engorgement or thickening of the vessels. In the gray matter of the cord in the mid-dorsal region the vessels appeared full and engorged, although there was no actual exudation round them. The posterior nerve-roots appeared normal. The cells of the posterior root ganglia also appeared normal but were considerably pigmented. The Marchi method showed no degeneration.

Peripheral nerves.—By the Marchi method there was some degeneration in the left sciatic and left anterior crural nerves, and more in the left than the right phrenic nerve. In the corresponding nerves of the right side the degeneration was equally marked, and by the Weigert-Pal method some atrophy of the nerve fibres could be seen.

Muscles.—The fibres of the left vastus internus muscle were fairly uniform in size, but were below the average of the normal muscle, measuring about ·04 mm. The transverse striation was well marked and there was no fatty change. The right vastus internus was in the same condition, the fibres measuring ·04 mm. in diameter. The striation was well marked and there was no fatty change.

Case 3.—S. D., a married woman aged 48 years, was admitted into the National Hospital under the care of Dr. Bastian on January 20, 1899, complaining of stiffness and numbness of the legs.

Three years before admission she began to suffer with a tumour in the left loin, and two years later the left kidney was excised for pyonephrosis. She recovered completely from this operation. With this exception her health had always been good. Several facts were elicited suggesting that she had had syphilis. She had not taken excess of alcohol.

Her illness began in September, 1898, when she first noticed weakness and stiffness and numbness in the legs. Shortly afterwards she fell downstairs, and subsequently had great difficulty in walking and had slight incontinence of urine. The legs gradually got worse and she became very pale. A girdle sensation appeared just above the umbilicus.

When admitted she was a very anæmic, sallow-complexioned woman. She was well nourished. Her mental state was reduced and her memory was poor. Speech, articulation, special senses, optic discs and cranial nerves were normal. The pupils were equal and reacted normally. The abdominal muscles below the umbilicus were very weak, and the umbilicus shifted upwards an inch in the attempt to sit up. All movements of the upper extremities were performed strongly. There was slight ataxy of the hands. All movements of the lower extremities were performed very feebly and were very ataxic. The legs were slightly rigid at all joints. There was no wasting. There was marked blunting of sensibility to all forms below the ninth dorsal root area. Complete loss of sense of passive position in the legs. She complained of shooting pains in the legs and of a girdle sensation just above the umbilicus. Slight incontinence of urine.

Reflexes.—Wrist, elbow, and jaw-jerks were brisk. Knee-jerks exaggerated. Double foot clonus. Superficial reflex excitability of the lower limbs much increased. Plantar reflexes were extensor responses.

Urine normal. Temperature ranged between 98° F. and 102·5° F. The spleen could not be felt. There was a loud hæmic murmur to be heard in the neck. No hæmorrhages were found. Blood count: Hæmoglobin 20 per cent., R.B.C.'s 1,800,000 per cm. Red cells all sizes and irregular in shape. No nucleated forms. Some Eichhorst's cells seen. There was a marked lymphocyte leucocytosis and no hyaline cells were seen.

A week after admission the legs became quite flaccid, the knee-jerks were lost, the anæsthesia and incontinence became complete, the muscles began to waste and to lose their faradic excitability, and œdema of the legs and trunk appeared, the extensor plantar reflexes remaining.

Under treatment with iron and arsenic the anæmia improved considerably, the hæmoglobin reaching as high as 50 per cent., but it gradually fell again to 20 per cent. The œdema disappeared. The lower extremities became extremely wasted, the muscles entirely losing their excitability to faradism; the diaphragm became paralysed. Bedsores developed. The patient died suddenly of syncope five weeks after admission.

Duration of illness—six months; stage of ataxic spastic paraplegia—four months; stage of flaccid paraplegia—two months.

Post-mortem Examination.

The body was fat, the limbs were flaccid. The brain showed some shrinking of the convolutions on the right side about the upper part of the ascending parietal convolution, but otherwise was normal. The spinal cord was somewhat shrunken and firmer than normal, and on section showed changes in the posterior and lateral columns. There was some fluid in both pluræ, and the bases of both lungs were considerably collapsed. The heart appeared normal. The liver was enlarged and weighed 60 ozs. Spleen was large and soft and weighed 12 ozs. The left kidney was absent (removed by operation). The right weighed 8 ozs. and was covered by small raised nodules (septic infarcts). The bladder showed cystitis. The muscles of the lower extremity were pale, flabby, and very watery; the biceps cubitis was of normal appearance.

Cortex.—Microscopical examination of the cerebral cortex both with regard to the cells, the medullated fibres, and the tangential fibres, showed no change in these structures.

Cerebellum and pons.—Both these appeared normal by the Weigert-Pal and Nissl methods, but by the Marchi method degenerate fibres could be seen in the ventral cerebellar tract and in the velum, but no other degeneration could be seen at this level.

Upper level of the medulla.—This region appeared normal by the Weigert-Pal method, but by the Marchi method degeneration could be seen in the restiform bodies and in the ventral cerebellar tracts, and there was also scattered degeneration throughout both pyramids. In the medulla the degeneration first became marked at the level of the posterior column nuclei by the Weigert-Pal method and was present in the pyramids, in the direct cerebellar tract, and in the funiculus gracilis and cuneatus. The same section stained by Marchi shows very considerable degeneration of a recent character in the direct cerebellar tracts and older change leading to vacuolation in the pyramids.

Spinal cord.—By the Weigert-Pal method the degeneration was most marked in the dorsal region of the cord, where it affected almost the whole of the white matter except a small zone immediately surrounding the gray matter. The sclerosis was rather more marked in the crossed pyramidal tracts than in the other parts of the cord in this region. In the cervical region of the cord the degeneration was less extensive and was more patchy in distribution—for instance, there were numerous irregular patches of sclerosis in the region of the direct pyramidal tract, while the portions of the cord external to this were less affected. In the upper cervical region the destruction wa smost marked in the posterior columns and in the cerebellar tracts. Passing then to the lower dorsal and lumbar region, it was found that there was some affection of the posterior columns down to the lower lumbar region, but the sacral was quite free. There was degeneration corresponding to the crossed pyramidal tracts in the lower dorsal, lumbar and sacral regions, and in the latter region it was the only degeneration present. By the Marchi method all the features as above described were present, but it was very striking how little recent degeneration, as evidenced by the presence of fat granules, was present, while the vacuolation and sclerosis of the cord were marked features, and it was only in the areas that appeared normal by the Weigert-Pal method that any number of recently degenerated fibres could be seen. The gray matter of the cord and the cells of the anterior horn and the cells of Clarke's column appeared normal. It could not be positively asserted that there was no change, nor that there was no diminution in the number of the cells of the anterior horns, but it could be asserted that there were numerous perfectly normal cells in the anterior horns in every region of the cord.

Sections stained by van Gieson's method showed that there was no inflammatory condition in the gray matter. In the areas in which the sclerosis of the cord was most marked the vessels were full and engorged and their walls were thickened, but there was no evidence of thrombosis, and in the normal regions of the cord the vessels were neither dilated nor thickened. There was no change in the pia-arachnoid membranes of the cord.

Anterior nerve-roots appeared normal both by the Weigert-Pal and by the Marchi method. The posterior nerve-roots also appeared normal by both methods.

Posterior root ganglia.—No change could be found in these either by the Nissl or Marchi methods. The cells were, however, extensively pigmented.

Peripheral nerves.—No change could be found in any of the following peripheral nerves which were examined by the Marchi and Weigert-Pal methods—right and left sciatic, median, anterior crural, and phrenics.

Muscles.—Right rectus femoris: The fibres of this muscle varied very greatly in size, the largest measuring only ·04 mm. in diameter and the average less than ·02 mm. The striation was well preserved. Left vastus internus: The description given above of the right rectus femoris will apply to this muscle. There was no fatty change within the muscle fibre. Right biceps: The fibres of this muscle were much less atrophied than those above described and were far more uniform in size.

Case 4.—M. D., a married woman, aged 39 years, was admitted into the National Hospital, under the care of Dr. Bastian, on August 16, 1899, complaining of general loss of strength and anæmia of two years' duration and of loss of power and feeling in the legs of six weeks' duration. Until this illness her health had always been good. No facts were elicited suggesting that she had had syphilis. She had indulged freely in alcohol. She lived in the same street as the patient S. D., in Case 3 just described.

Two years before admission, without any assignable cause, she lost her strength, and became very pale and breathless. Her medical attendant found that she was suffering from severe anæmia and irregular pyrexia. She remained confined to bed for six months, and then slowly got better, but never regained her original strength.

Three months before admission she first noticed numbness, weakness, and unsteadiness in the legs. These symptoms increased, but she was able to get about and to do her housework till a week before admission. During this time she had severe shooting-pains in the legs and had a constant heavy pain beneath the left costal margin, and a girdle sensation just below the ensiform process.

A week before admission she became unable to stand, the legs and hands became very numb; she had incontinence of urine, œdema of the legs, and several fainting attacks. The legs at this time became very stiff.

When admitted she was a well-nourished woman. The skin was very pale and sallow. Her mental state was one of extreme exhaustion, and she was delirious at night. Temperature from 98° F. to 101° F. Speech, articulation, special senses, optic discs, and cranial nerves were normal. The pupils were equal, and reacted normally. The abdominal muscles and lower part of the erectores spinæ were very weak. She could not sit up in bed or maintain the sitting posture when raised. The movements of the upper extremities were feeble, and there was marked incoordination. There was some fine tremor of the fingers. The lower extremities were flaccid, and all movements were extremely feeble; great incoordination and marked hypotonia; some general wasting. All the muscles of the lower extremities showed great diminution of excitability to faradism and galvanism; A. C. C. > K. C. C. She complained of occasional shooting-pains in the legs and of a severe dull pain beneath the left costal margin. There was a tight girdle sensation at the level of the ensiform process.

There was distinct diminution of sensibility to all forms, evenly distributed below the fourth dorsal root level and over the eighth cervical and first dorsal root areas. There was complete loss of sense of passive position in the lower extremities, and marked loss in the hands. There was reflex incontinence of both sphincters.

Reflexes.—Wrist, elbow, and knee-jerks absent. The plantar reflexes showed the extensor response. The superficial reflex excitability of the lower limbs was much exaggerated.

Heart.—There was a soft apical systolic murmur and a loud venous hum in the neck. The pulse was regular and of low tension. Blood count, August 20: Hæmoglobin, 56 per cent.; red blood cells, 4,000,000 per cm.; no poikilocystosis; no nucleated red cells; a few Eichhorst's cells; white cells normal. There were no hæmorrhages. She was treated with arsenic, strychnine, and iron.

On August 21 she had a syncopal attack, and in the course of the next half-hour the right upper extremity became very œdematous as high as midway between the elbow and shoulder. Four hours later the œdema of the arm had completely disappeared.

She left the hospital against advice on August 24, but was readmitted on September 16 profoundly anæmic and with a large sacral bedsore.

Blood count on October 2: Hæmoglobin, under 20 per cent.; red blood cells, 800,000 per cm.; marked poikilocystosis; no nucleated red blood cells; no Eichhorst's cells; ratio of white cells to red, 1 to 40. There was marked increase in the number of lymphocytes. No coarse oxyphile or hyaline cells were seen in stained specimens.

There was then marked œdema of the lower extremities and of the hands. The upper extremities were almost completely paralysed, and the muscles only reacted to strong faradic stimulation. There was complete flaccid palsy, with great wasting, loss of faradic excitability, and polar change in the muscles of the lower extremities. There was almost complete anæsthesia to all forms below the seventh cervical root area, and absolute anæsthesia below the fourth dorsal root level. There was complete incontinence of both sphincters. The deep reflexes were absent; the plantar reflexes were still extensor responses. She was constantly delirious; the temperature remained above normal; and she died of respiratory failure on October 19.

Duration of illness: Anæmia—two years; nervous symptoms—five months; stage of spastic paraplegia—ten weeks; stage of flaccid paraplegia—ten weeks.

Post-mortem Examination.

Body well nourished and fat; the limbs were flaccid. There was a bedsore over the sacrum. The brain was normal; the spinal cord appeared normal on its external surface, but on section showed degeneration of the lateral and posterior columns. The heart was flabby and appeared fatty, but the valves were normal. The lungs were very œdematous. The liver was large, weighed 67 ozs., and was friable and fatty. On testing it for free iron a reaction developed which was inconclusive, but subsequent microscopical examination showed that none was present. The spleen weighed 16 ozs., and was diffluent. The kidneys were slightly granular, but were otherwise normal. The bladder appeared fairly normal. The bone marrow of the femur was of a dark red colour, almost diffluent, and very like the spleen in consistency. The muscles were pale, flabby, and very watery.

Microscopical Examination.

Cortex cerebri.—This was normal both as regards the cells, medullated fibres, tangential fibres, and the Marchi method revealed no degeneration. Cerebellum and pons appeared normal.

Medulla.—The upper portion of the medulla appeared normal by the Weigert-Pal method. By the Marchi method, however, degenerated fibres could be seen in both direct cerebellar tracts and in the restiform bodies. At the level of the decussation there was considerable degeneration in both cerebellar tracts, in both the funiculus gracilis and cuneatus, and in the pyramids, as shown both by the Marchi and Weigert-Pal methods.

Spinal cord.—By the Weigert-Pal method there was degeneration of the posterior columns from the lumbar to the cervical region; the destruction was most marked in the dorsal region, somewhat less in the cervical, still less in the lumbar, while the sacral region escaped altogether. The areas of degeneration were rather patchy, but in the cervical region the degeneration was more marked in the column of Goll than in the column of Burdach. There was degeneration in both lateral columns of the cord especially marked in the peripheral portions of the cord in dorsal region. The degeneration in the pyramids could be traced from the cervical to the sacral region, but below the mid-dorsal region it assumed the character of a descending degeneration. The direct cerebellar tract was degenerated, and could be traced up to the restiform body. The fibres in immediate relation with the gray matter appeared fairly normal. The recent degeneration as shown by the Marchi method was very slight, and the areas which showed most fatty granules were those belonging to the long tracts of the cord. The cells of the anterior horn were somewhat pigmented, but otherwise appeared normal; and the cells of Clarke's columns also were normal.

Vessels.—In the regions of the cord where the sclerosis was most marked there was thickening of the walls of the vessels which affected chiefly the middle coat. In the normal portions of the cord the vessels appeared normal.

Posterior roots.—These appeared perfectly normal.

Posterior root ganglia.—The cells of these ganglia were well formed and appeared normal, though there was rather a large amount of pigment present.

Peripheral nerves.—The following nerves were examined and appeared normal:—The right anterior crural and the branch to the right vastus internus muscle, the nerve to the left rectus femoris, and the left sciatic.

Muscles.—The muscle fibres of the right vastus internus were considerably atrophied, the average diameter being somewhat under ·04 mm.; there was no fatty change within the muscle fibres, and the striation was well marked. The muscle fibres of the left rectus femoris were of irregular size, and averaged about ·032 mm. in diameter, and the striation was well marked.

Liver.—No free iron could be detected in the liver. There was a good deal of fat, but not more than is often found in the livers of persons dying of wasting diseases.

Kidneys.—These appeared normal.

Case 5.—E. F., a married woman aged 49 years, was admitted into the National Hospital under the care of Dr. Hughlings Jackson on December 23, 1898, complaining of loss of power in both legs, sphincter trouble and bedsores.

The family history was unimportant. Previous to this illness her health had been good; there was no history of syphilis and she had always been most abstemious as regards alcohol.

The history of the illness was as follows:—A year before admission the legs became numb and weak and were easily tired. Soon after she dragged the legs in walking and was unsteady when standing, and had occasional diplopia. For ten months she remained able to do her work, but at the end of this time she rapidly became quite unable to stand, and had severe shooting pains in the legs.

A month before admission the legs, which up to this time had been stiff, became quite flaccid, she completely lost control of the sphincters and developed œdema of the legs and trunk, and a large bedsore made its appearance.

When admitted she was a well-nourished, healthy-looking woman. She was not in the least anæmic. She was quite unable to move the legs and trunk, she was completely incontinent, and there was a large sacral bedsore. She had severe cystitis, and the temperature was 102° F. By day she was mentally clear, but at night there was noisy restless delirium. Speech, articulation, special senses and optic discs were normal. The pupils were equal and reacted normally. There was marked weakness of both external recti. The abdominal muscles were completely paralysed below the umbilicus. The upper extremities were slightly tremulous, but were otherwise normal. There was complete flaccid palsy of the lower extremities. All the muscles were much wasted. None of the muscles of the lower extremities reacted to faradism and the reaction to galvanism was very feeble. There was absolute loss of sensibility to all forms below the first lumbar root level, and marked impairment to all forms as high as the tenth dorsal root level. There was complete loss of sense of passive position in the lower extremities and some impairment in the hands and fingers. There were some trophic changes in the skin of the feet. There was complete incontinence of both sphincters and severe hemorrhagic cystitis.

Reflexes.—The wrist and elbow-jerks were exaggerated. The knee-jerks were totally absent; there was no foot clonus, but two months before admission she had been seen by Dr. Tooth, and he had made a note that at that time the knee-jerks were exaggerated and that there was double foot clonus. There was much soft œdema of the legs and lower part of the trunk. The spleen was not palpably enlarged. There was no anæmia. The other organs were examined and found healthy. She died comatose thirteen days after admission.

Duration of symptoms—thirteen months; stage of slight ataxic paraplegia—ten months; stage of severe paraplegia—one month; stage of flaccid paraplegia, absent knee-jerks and œdema —six weeks.

Post-mortem Examination.

Body well nourished, excess of adipose tissue, bedsore over sacrum. All the organs of the body appeared normal except the spinal cord, which showed on section distinct changes in the posterior, antero-lateral and anterior columns.

Microscopical Examination.

Cerebral cortex appeared normal both as regards its cells and the tangential fibres, and no degeneration could be seen by the Marchi method. Cerebellum was normal.

Pons.—There were scattered degenerate fibres in both pyramids in the pons and in the superior cerebellar peduncles. By the Weigert-Pal method the pons appeared normal.

Medulla.—There were scattered degenerate fibres throughout both pyramids and both restiform bodies as seen by the Marchi method.

Lower level of the medulla.—Degeneration of both direct cerebellar tracts was most marked, there was scattered degeneration in both pyramids and also in the funiculus gracilis and funiculus cuneatus, but more marked in the former than in the latter. By the Weigert-Pal method some change could be seen in the direct cerebellar tracts and in the posterior columns, but the pyramids appeared normal.

Spinal cord.—By the Weigert-Pal method the degeneration was most marked in the dorsal region of the cord, affecting the posterior and crossed pyramidal tracts to the greatest extent, leaving the ventral portion less affected. In the cervical region the posterior columns were more affected than the lateral, while in the lumbar region the lateral columns were more affected than the posterior. The process in this case would seem to be much less destructive than in some of the other cases, there being more recent degeneration and more sclerosis, but less vacuolation; the distribution of the degeneration is, however, the same. By the Marchi method there was in the cervical region marked degeneration in the posterior columns, especially in Burdach; the columns of Goll were so sclerosed that they showed little recent degeneration. Degeneration was also present in the pyramidal and direct cerebellar tracts, and in a few fibres in the ventral columns of the cord, while in the lumbar region some degenerate fibres could also be seen in the posterior column and in the ventral region of the cord. In the sacral region there was degeneration in the crossed pyramidal tracts alone.

Van Gieson's method: The gray matter appeared normal. The vessels in the affected areas were thickened and engorged, but were not thrombosed; in the unaffected areas of the cord they appeared normal.

Nissl method: The cells of the cervical and dorsal region of the cord were possibly fewer in number than normal, but those remaining were well stained and appeared normal. The cells in the lumbar region appeared perfectly normal. The cells were considerably pigmented.

Peripheral nerves.—The following peripheral nerves were examined and were found to be perfectly normal both by the Marchi and Weigert-Pal methods—the right and left sciatic, left anterior tibial, the nerves to the right and left vastus internus muscles, and the nerves to the right and left vastus externus muscles.

Muscles.—Right rectus femoris: The fibres of this muscle are somewhat atrophic, averaging about ·04mm. in diameter; they are well striated and show but slight fatty change within the fibres. Right vastus externus muscle: The fibres vary greatly in size, having a rounded instead of polygonal outline; there were several degenerate fibres scattered throughout the muscle, which showed black granules when stained by osmic acid; these fibres are not numerous, and are always of small size, ·02—·03mm. Right vastus internus muscle exhibited the same condition as the above two muscles. It is very noticeable, however, how few nerve-fibres there are in the muscle tissue when stained by Pal's method when compared to the normal. When, on the other hand, one compares the condition with that found in case No. 1, in which, in spite of the extreme atrophy of the muscle, the nerve-fibres are well preserved, one cannot but think that the absence of nerve-fibre in this portion of the muscle is a fortuitous condition.

Case 6.—Ruth M., aged 45 years, was admitted into the National Hospital under the care of Dr. Hughlings Jackson on June 30, 1897, complaining of paralysis of the legs and sphincter trouble. There was a history of epilepsy, cancer, and of phthisis in the family. She had been a strong, healthy woman, and she had probably had syphilis. She had been addicted to alcohol. A very incomplete history of the illness was obtained owing to the patient's mental state and the absence of any friends who were in a position to give a detailed history.

Her illness dated from six weeks before admission, when she began to complain of numbness of the hands and feet, stiffness of the legs, and difficulty in walking.

A fortnight later she became unable to stand, developed a girdle sensation and sphincter trouble. She had frequent fainting attacks, and several attacks of general convulsions, in which she lost consciousness and passed urine.

When admitted she was a poorly nourished woman, unable to stand or walk. There was some mental obfuscation. Speech, special senses, optic discs, and cranial nerves were normal. The pupils were irregular, and there were anterior synechiæ in both eyes. The upper extremities showed some slight incoordination, but were otherwise normal. The respiratory muscles and erectores spinæ were normal; the lower half of the abdominal muscles were weak. Both lower limbs were rigidly extended and were completely paralysed. There was diminution of sensibility to all forms below the ninth dorsal root level, and a tight girdle sensation at this level. There was distension of the bladder with overflow.

Reflexes.—Wrist and elbow-jerks increased; knee-jerks exaggerated. Double foot clonus. Superficial reflex excitability increased in the legs. Plantar reflexes brisk. Marked anæmia. Blood not examined. Liver and spleen not palpably enlarged.

After admission the temperature remained above 101° F. She was constantly delirious. The legs became flaccid, the knee-jerks disappeared, and slight œdema of the lower extremities appeared. The anæsthesia became absolute, the sphincters completely incontinent, and she died much emaciated seven weeks after admission.

Duration of illness—fourteen weeks; stage of spasticity—eleven weeks; stage of flaccidity—three weeks.

Body much emaciated. Brain: the convolutions were somewhat shrunken and there was slight compensatory œdema, otherwise normal. Spinal cord was normal to external appearances, but on section showed sclerosis of the posterior and lateral columns. The heart was natural. The lungs were œdematous. Liver was large and firm, and there was evidence of old perihepatitis. The kidneys were normal.

Microscopical Examination.

Sections of the medulla and spinal cord showed by the Weigert-Pal method that at the level of the pyramidal decussation there was extensive degeneration of the fibres of the posterior column nuclei and of the lateral region of the medulla in the area occupied by the cerebellar tracts, in addition to which there were two small areas symmetrically placed in the antero-lateral region of the medulla. Moreover, a patchy degeneration was evident in the pyramidal fibres at the decussation. The upper cervical cord was the seat of complete degeneration of the posterior columns except the part bordering on the gray matter. There was extensive degeneration of the lateral columns, but the ventral portion of the cord was preserved. In the lower cervical cord a similar condition was present but to a less marked degree, in the dorsal portion of the posterior external column, while the lateral column degeneration was more extensive, and there was here patchy degeneration in the region of the direct cerebellar tracts, though not confined to these. In the thoracic cord the posterior degeneration was as extensive as in the upper cervical region, and in the lateral areas of the cord more extensive than at the higher levels, as was also the degeneration of the direct pyramidal tracts, which obviously extended beyond the strict limits of these. The only parts of white matter preserved were those bordering on the gray. In the lower thoracic region some fibres in Goll's column were preserved, and there was less extensive degeneration in the ventral parts of the cord. In the lumbar region there was no degeneration in Goll's column, but some in Burdach, especially in the peripheral portion, while the whole of the ventral portion of the cord was preserved.

The Marchi method revealed scattered degenerated fibres in the pyramids, in the lateral region of the medulla in the parts occupied by the cerebellar tracts, and also in the restiform body, but not confined to the area normally occupied by these tracts. There were degenerate fibres in the posterior column nuclei. The condition found in the spinal cord confirmed the findings by the Weigert-Pal method. The great feature of the Marchi specimens was not so much the bringing into evidence of recently degenerated fibres, of which there are comparatively few, but the making evident of spaces by the falling out or absorption of the destroyed fibres. Fibres that still stain black are seen in the less affected parts, *e.g.*, in the white matter bordering on the gray. The parts of the cord most destroyed were the postero-lateral and ventral, the part between these two areas in the antero-lateral region being less affected. In the upper sacral region there was some falling out of the fibres in the neighbourhood of the ground bundles, but there were scarcely any black fibres. In the lower sacral region no change was found except a few black fibres on each side of the posterior median septum. No descending degeneration was evident, in spite of the lateral columns being extensively destroyed in the lumbar region of the cord.

Case 7.—S. W., aged 38 years, was admitted into the National Hospital, under the care of Dr. Bastian, on November 23, 1899, complaining of paralysis and numbness of the legs, swelling of the legs, and loss of control over the sphincters. There was a strong family history of tubercular disease. He had been a strong healthy man. He had had syphilis when 22 years old, and had been a heavy beer drinker. A year before this illness commenced he suffered with inflammation of the bladder.

Three years before admission he caught a chill, and directly afterwards noticed that his feet felt numb and stiff. During the next two years the numbness gradually crept up the legs and invaded the trunk, and he was unsteady and dragged his legs in walking, but he kept at his work without much difficulty.

Six months before admission he suffered with severe shooting-pains in the legs. His legs became very stiff, and he became much more unsteady, could not walk in the dark, and fell into his basin when washing. At this time he was a patient at Charing Cross Hospital, where the presence of double foot clonus and increased knee-jerks was noticed.

He remained in this condition without the development of further symptoms till six weeks before admission, when in the course of a few hours he became unable to stand, and for the first time during his illness lost control of the sphincters; this loss remained complete. The loss of sensibility of the legs and trunk became much more severe; he became very pale in the face, and œdema of the legs appeared. He developed cystitis, and became delirious at night.

When admitted he was a pale, sallow-faced, sparely-nourished man. The skin had a waxy-yellow appearance. He lay on his back in bed, unable to move the legs or trunk. He was delirious at night, and his temperature was 102·5°. He had severe cystitis and much hæmorrhage from the bladder. His mental state was facile, and he had varied delusions. On two occasions he had an attack of general convulsions lasting ten minutes, during which time he was comatose. The special senses and cranial nerves were normal. The retinal fundi were yellow in colour, and there were a few small hæmorrhages. The pupils were small and equal; they reacted normally. The erectores spinæ and abdominal muscles did not contract on attempting to sit up or on the attempt to move the trunk. The lower intercostals moved badly in respiration; the diaphragm acted well. All movements of the upper extremities were performed feebly and with marked ataxy. The weakness was more marked in the periphery and the intrinsic muscles of the hands, and the ulnar flexors were markedly wasted. In these muscles faradic excitability was much diminished; to galvanism, K. C. C. > A. C. C. There was absolute paralysis of the lower extremities, with slight flexor and adductor spasm. There was some rigidity at all joints, but the muscles hung loosely on the bones and were flabby. There was no wasting. There was some diminution to faradism below the knees. There was a severe girdle pain round the lower part of the chest and some shooting pains in the legs. There was complete analgesia to all forms of moderate stimuli from the upper limit of the first lumbar root distribution. Light touches and pricks were not felt below the fifth dorsal root level. There was complete loss of sense of passive position in the lower extremities and marked loss in the joints of fingers and hands. Absolute incontinence of both sphincters. Severe cystitis. Cranium and spine normal. Severe bedsore on left hip. The knee-jerks were exaggerated; no foot clonus; wrist and elbow-jerks brisk. The plantar reflexes were brisk extensor responses, and there was some dorsal retraction of the great toes. The reflex excitability of the lower extremities was greatly exaggerated. There was marked breathlessness on slight exertion; loud basic systolic murmur and *bruit de diable*. Pulse, very low tension. Blood count: Hæmoglobin, 30 per cent.; red blood cells, 1,600,000 per cm.; white blood cells; a marked lymphocyte leucocytosis; very few hyaline cells seen; all other normal forms seen; no poikilocytosis; no microblasts, normablasts, and no gigantoblasts; no Eichhorst's cells found. There was no palpable enlargement of the spleen or of the lymphatic glands. No œdema was present at the time of admission. No abnormality was found in the other organs.

During the first week after admission the clinical picture changed remarkably; the deep reflexes disappeared, and were never again obtained. The spastic condition of the lower limbs gave place to one of complete flaccidity. The muscles of the legs and hands wasted rapidly and lost their faradic excitability within a few days. The excitability to galvanism and to percussion were almost abolished. Much soft œdema of the legs and back appeared, and lasted about three weeks. A heavy constant pain was complained of in the left hypochrondriac region. The cystitis was soon cured with appropriate treatment, and the bedsore healed. Following a severe attack of pain in the left side, a cutaneous hæmorrhage, precisely limited to the area of distribution of the seventh left dorsal root, appeared with two smaller patches over the tenth and eleventh left dorsal root areas. Trophic changes in the skin, similar to those seen in neuritis, occurred in the four extremities. The wasting of the muscles was progressive, and the diaphragm became paralysed.

The plantar reflexes constantly were extensor responses, and the superficial reflex excitability of the lower limbs remained excessive.

Death occurred from exhaustion.

Post-mortem Examination.

The body was extremely thin and wasted, there was a sloughing bedsore over the sacrum, and the scar from an old hæmorrhage in the area corresponding to the seventh thoracic root of the left side. The skull and membranes of the brain were normal. The convolutions of the brain appeared normal, and the cranial nerves and the vessels were natural.

Spinal cord.—There was some purulent exudation on the outer surface of the dura mater in the lower part of the spinal canal arising from the bedsore over the sacrum. The external appearance of the cord was natural, there was no wasting, and the anterior and posterior roots appeared of normal size. There was no meningitis or thickening of the pia-arachnoid. On section the gray areas of degeneration were distinctly visible. The lungs were healthy except for some œdema at the bases. The heart was normal. The diaphragm was natural. The liver was slightly enlarged and gave no free iron reaction. The spleen was enlarged, soft and pulpy. The kidneys showed considerable pyelitis, and the infective infarcts were more numerous in the right than in the left. The bladder contained some purulent urine, and showed a condition of chronic cystitis. The bone marrow of the right femur was examined and appeared pale and of normal consistence. The muscles were wasted, but were not very pale nor œdematous. The right sciatic nerve was evidently very fatty. The posterior root ganglia appeared normal to the naked eye except the seventh left dorsal, and on making an incision into this, after it had been hardened in formalin it was found to contain a small cyst measuring about 3 mm. in diameter, and this contained a little clear fluid,

Microscopical Examination.

By the Weigert-Pal method the cortex appeared normal, the tangential fibres were well stained, the pons and upper levels of the medulla also appeared normal. In sections taken through the lower portion of the olive some change could be seen in the pyramidal tracts, and there was considerable vacuolation in this area; the direct cerebellar tract was similarly affected. In sections below the level of the posterior column nuclei degeneration could be seen in the funiculus gracilis and funiculus cuneatus, the direct cerebellar tract, and in both pyramids. At the level of the decussation of the pyramids there was marked degeneration of the posterior columns, both internal and external, and also of the direct cerebellar tracts; both pyramids were also markedly affected. In the upper cervical region there was extensive sclerosis of the posterior columns, the direct cerebellar tract, and also very considerable affection of the pyramids, but though most marked in these is not limited to them. The nearer the sections examined to the mid-dorsal region the more extensive was the sclerosis, and it was no longer limited to the tracts above-mentioned but affected the whole of the periphery of the cord, leaving the gray matter and a small band of medullated fibres that immediately surrounded it alone normal. At the level of the twelfth dorsal the posterior columns were still markedly affected, but there was less degeneration in the ventral portion of the antero-lateral tracts, the degeneration of the pyramids was still marked. In the lumbar region the posterior columns still showed considerable degeneration, and there was degeneration both in the region of the direct and crossed pyramidal tracts, although it was not strictly limited to the tracts.

Marchi method.—In the cortex there were a few degenerate fibres in the white matter, and these could be traced down into the crura, being rather more numerous on the one side than the other. In the pons degenerate fibres could be seen in both pyramids and in the ventral cerebellar tract, and in addition to this there was a small area of softening with degenerate fibres just ventral to the posterior longitudinal bundle. In sections taken through the upper part of the medulla, scattered degenerate fibres could be seen in the pyramidal tracts, and in the direct cerebellar tracts these were more numerous and could be seen passing into the restiform bodies. Scattered degenerate fibres could also be seen in the region of the posterior column nuclei. In sections taken through the medulla at a lower level, scattered degenerate fibres could be seen in both pyramids, the direct cerebellar tract, and in the funiculus cuneatus, the degeneration being more marked in the last-named tract than in either of the other two. Very few recently-degenerate fibres could be seen in the funiculus gracilis, owing to it being extensively sclerosed. At the level of the decussation the same features as described in the above section were present. In the cervical region of the cord the recently-degenerate fibres were more scattered, and did not form such definite tracts as in the sections at higher levels. In the dorsal region there was considerable degeneration all round the periphery of the cord, and the portions where the degeneration was of longest standing, viz., the columns of Goll, and the crossed pyramidal tracts showed fewer recently-degenerate fibres than the other portions of the cord. In the upper lumbar region the degeneration again became less, being most marked in the posterior columns and in the ventral region of the cord that lies on either side of the median fissure. In the sacral region the vacuolation, which had been a marked feature through the cervical and dorsal regions, had disappeared from all parts of the cord except the posterior columns, where it was still present to a slight degree; recently-degenerate fibres were still present both in the posterior and ventral region of the cord. In the coccygeal region a few degenerate fibres could be seen in the posterior columns at the most dorsal portion on either side of the median fissure.

Nissl method.—The cells of the cortex, pons, or medulla appeared for the most part normal; there were fairly numerous healthy cells in every region of the cord, but in the lumbar region, although they have a good nucleus and nucleolus, the cells were somewhat swollen and the chromophilic substance rather finely granular. Some of the cells were pigmented, but not to a marked degree. It is probable that there was some diminution in the number of cells in the anterior horn. The cells of Clarke's column were few in number, stained badly, and were markedly pigmented.

Van Gieson's method.—Sections stained by the above method taken at various levels in the medulla and spinal cord were examined with regard to the condition of the vessels and membranes. With regard to the latter no thickening could be found in any region of the cord; the vessels in the pia arachnoid were in some parts distended with blood, but there was no evidence either of recent or of old thrombosis. With regard to the vessels within the cord in those portions which were most affected, the vessels were often engorged, but there was no thickening of the walls or evidence of thrombosis. There was no small cell infiltration around the degenerate areas, whether recent or old.

Peripheral nerves.—The right sciatic showed marked degeneration by the Weigert-Pal method, more than one-half of its fibres having undergone degeneration. The same feature was apparent by the Marchi method, but the number of recently degenerate fibres was small, although in one bundle this was fairly marked. The right anterior crural nerve was very much better preserved than the sciatic, comparatively little degeneration being visible by the Weigert-Pal method. By the Marchi method, however, although there was practically no recent degeneration the spacing of the fibres showed that a considerable number of fibres must have undergone atrophy. The right phrenic nerve appeared normal both to the Weigert-Pal and to the Marchi method.

Posterior root ganglion.—The cells of the posterior root ganglion were for the most part normal, although here again some were considerably pigmented, and others were shrivelled. The seventh left thoracic posterior root ganglion showed on section a small cyst measuring 3 mm. in diameter and filled with a clear fluid (plate ix., fig. 2). The walls of this cyst were laminated, the inner layer being formed of fine connective tissue and the outer layers of more closely packed fibrous tissue. Many of the cells of the ganglion appeared atrophied and pigmented, others, however, were normal. There was an increase of connective tissue between the cells. The anterior and posterior roots, both by the Weigert-Pal and Marchi methods, appeared normal.

(This case has not been examined with the completeness of the other cases owing to the fact that the patient only died shortly before the publication of this paper; but sufficient has been done to show that it was a typical case of the disease, and owing to the long third stage corresponded closely to Case No. 1 in its pathological aspect.)

CASES NOT VERIFIED.

Case 8.—M. C., aged 38 years, a married woman, was admitted into the National Hospital under the care of Dr. Ferrier on September 23, 1898, complaining of weakness of the legs, numbness, and inability to walk. She had had syphilis ten years before admission, otherwise she had had good health. There was no history of alcoholic excess. Eighteen months before admission she first noticed numbness and stiffness in the calves of both legs. A few months later she dragged both feet in walking, the legs were stiff, and she had a tight girdle sensation round the waist. These symptoms gradually increased until six weeks before admission, when, in the course of one day, she became entirely unable to stand. With this she developed retention of urine (she had had slight precipitancy of micturition ever since the beginning of the illness).

Her doctor informed one of us (J. C.) that a month before admission he had examined her, and had found the knee-jerks brisk and double foot clonus present.

When admitted she was a very pale, sparely-nourished woman; the mental state, speech, articulation, special senses, optic discs and cranial nerves were normal. There was slight lateral nystagmus. The upper extremities and trunk were normal as regards motion. The lower extremities were well nourished and were flaccid. She could execute all movements of the lower extremities against fair resistance as she lay in bed. On attempting to walk, supported on either side, the feet were poorly lifted, and she was wildly ataxic. When standing supported much *danse des tendons* appeared. She fell at once when unsupported. The electric excitability of the muscles was normal. There was slight blunting of sensibility to touch and temperature, but not to pain over the lower two lumbar and all the sacral areas. Sense of passive position was entirely lost in the lower extremities, and was very much impaired in the wrists and fingers. The sphincters showed alternating retention and precipitancy.

Reflexes.—Wrist and elbow-jerks brisk. Knee-jerks absent. General reflex excitability of the lower limbs increased. Plantar reflexes showed extensor responses.

Blood count: Hæmoglobin 60 per cent. of the normal; red blood-cells 4,900,000 per cm.; no nucleated red corpuscles; white blood-cells normal. Spleen not enlarged. Other organs healthy.

She left hospital a month later, her condition not having changed. A month after leaving hospital she developed complete anæsthesia and severe œdema of the lower extremities, which became completely paralysed. Bedsores developed, and she died a month later.

No autopsy was performed.

Duration of illness—twenty months; stage of slight ataxic paraplegia—sixteen months; stage of severe paraplegia—two months; stage of flaccid palsy, absent knee-jerks, and œdema—two months.

Case 9.—H. T., a dressmaker, aged 30 years, was admitted into the National Hospital under the care of one of us (J. S. R. R.) on October 31, 1899, complaining of numbness and weakness of the legs, sphincter trouble, and anæmia, of one year's duration.

There was a family history of rheumatic fever. She had never been strong, and had frequently suffered with dyspepsia and anæmia. A year before admission she noticed that she was unsteady when walking in the dark, and she became very pale. This was followed by numbness in the legs, which became stiff and dragged when she walked. She got about till nine months later, when she became much worse, and was unable to walk. Numbness in the tips of the fingers and a girdle sensation then appeared. She became very breathless and pale, but had no hæmorrhages. Ten days before admission she developed complete incontinence of both sphincters.

When admitted she was an extremely anæmic, sparely-nourished girl. Her mental state was weak and emotional. Speech was normal, but her voice was low pitched, and she did not control the blast of air properly. She had been deaf in the left ear for ten years and had tinnitus on that side; otherwise the special senses were normal. Optic discs and cranial nerves (except tenth and eleventh) normal; the pupils were normal; there was slight lateral nystagmus. There was general paresis of the left vocal cord. The trunk muscles were normal. Movement of the upper extremities was generally feeble, and there was distinct ataxy in both upper limbs. All movements of the lower extremities were very feeble. She could just stand when supported on both sides. Great rigidity of the legs and some general wasting. The faradic excitability was diminished. Marked flexor and adductor spasm. There was slight numbness in the finger tips of both hands and a tight girdle sensation round the lower part of the abdomen. There was marked impairment of sensibility to all forms below the root level—nowhere absolute. Severe dull pain in left hypochondrium.

Reflexes.—Jaw-jerk not obtained. Wrist and elbow-jerks exaggerated; knee-jerks exaggerated; double foot clonus. Superficial reflex excitability of the lower extremities much increased; plantar reflexes were brisk extensor responses; abdominal reflexes absent. Complete incontinence of both sphincters. Spine normal. Heart: Loud basic systolic murmur; *bruit de diable.* Liver and spleen not palpably enlarged. Some soft œdema of lower limbs and back. Blood count: Hæmoglobin, 68 per cent.; red blood cells, 4,700,000 per cm.; a few nucleated red cells present; no poikilocytosis; marked lymphocyte leucocytosis. The temperature ranged between 99° and 102° F.

This patient subsequently developed patches of herpes over the fifth left dorsal root area, and the anæsthesia crept up to the upper limit of the seventh cervical root area.

On November 17 the blood was again examined, with the following result:—Red blood cells, 3,708,000 per cm.; white blood cells, 7,000 per cm. No nucleated red cells. Differential leucocyte count:—(*a*) Polymorphonuclear cells, 71 per cent.; (*b*) lymphocytes, 23 per cent.; (*c*) hyaline cells, 3 per cent.; (*d*) coarse oxyphile cells, 1·2 per cent.; (*e*) basophile cells, 0·6 per cent.; (*f*) cells with reniform nuclei, 1·2 per cent.

We are much indebted to Dr. A. G. Phear and to Dr. A. J. Whiting for valuable assistance in examining the blood of this patient.

Case 10.—A. T., a married woman, aged 37 years, was admitted into the National Hospital under the care of Dr. Buzzard on February 6, 1900. She complained of weakness and numbness in the legs and arms and inability to stand of seven months' duration. There was no history of syphilis or of alcoholism.

Seven months before admission she noticed that the feet were numb and slightly swollen. Soon afterwards the legs gradually became stiff and dragged when she walked, sometimes giving way at the knee. She did her work for five months. Two months before admission she became unable to stand and her arms became weak. She had had no ocular or sphincter trouble and no pain.

When admitted she was a well-nourished woman, not obviously anæmic. Mental state intelligent. Speech, special senses, optic discs and cranial nerves normal. There was slight incoordination in both hands, but no weakness or wasting. The trunk muscles were normal. All movements of the lower extremities were performed with considerable power, but with great incoordination. She could only stand when supported on both sides, and made the wildest excursions with her legs in attempting to walk. There was no wasting, and the electric excitability was normal. She complained of numbness in the legs and fingers. She could not recognise light touches below the fourth lumbar root level. There was no sphincter trouble. The wrist and elbow jerks were difficult to elicit; the left knee-jerk was obtained with double reinforcement; the right was absent. The plantar reflexes showed a brisk extensor response.

Case 11.—J. M., a married woman, aged 54 years, was admitted into the National Hospital under the care of Sir William Gowers on August 4, 1899, complaining of weakness of the legs and of tingling and numbness in all four extremities. Her health previous to this illness had always been good. She had led an irregular life as an actress.

Two years before admission she had an attack of inflammation of the eyes, and herpes appeared all around the right eye. Shortly after this the legs and the fingers became numb; she had burning pain in the feet and a feeling as if she was walking on cotton wool. The legs slowly became stiff and she dragged them. The numbness spread slowly upwards, and she had a tight girdle feeling at the level of the umbilicus. She became very unsteady in walking.

Four months before admission she developed ptosis on the right side which passed off in a few weeks.

A month before admission she began to have difficulty in passing urine.

On admission she was a well-nourished, pale, sallow-complexioned woman. Mental state and speech normal. Smell was very defective in both nostrils, but otherwise the special senses were normal. The pupils were equal and reacted normally. The cranial nerves were normal to objective tests, but she stated that her voice in speaking and in singing had deteriorated very much during the year preceding admission. All movements of the upper extremities were powerfully performed, but with some incoordination, and there was some tabetic athetosis when the hands were held out and the eyes shut. The lower extremities were weak in all movements and there was marked ataxy. She could only stand with support on both sides, and on the attempt to walk the feet were raised high and placed down forcibly and in any position. The abdominal muscles were very weak, and she could not raise herself into the sitting position without assistance. There was marked diminution of sensibility to all forms below the ensiform process. The same diminution was found over the hands and ulnar borders of the forearms. She complained of a sensation like iron bands round the pelvis and abdomen as high as the lower costal margin. There was complete loss of sense of passive position in the lower extremities and marked loss in the hands. There was occasional incontinence of urine and constant delayed micturition. Wrist and elbow-jerks present and equal; knee-jerks increased; double foot clonus and the plantar reflexes showed the extensor response. Blood count: red blood-cells 4,300,000 per cm.; hæmoglobin 80 per cent.

Case 12.—W. P., a scene-shifter, aged 45 years, was admitted into the National Hospital under the care of Dr. Ferrier on March 21, 1898, complaining of weakness of the legs and of the right hand. Family history and previous health good. He was a scene-shifter, and worked in an atmosphere laden with colour dust from the scenery. He denied venereal disease. He was in the habit of taking a good deal of alcohol.

Seven weeks before admission he noticed a numb cold feeling in both feet, which rapidly spread up to the waist. The legs then became weak and stiff, and he dragged them in walking. Sudden flexor spasms in the legs troubled him at night. Six weeks later he was much worse, and the right hand became very weak. Sharp stabbing pains in all four limbs troubled him greatly.

On admission he was a strongly-built man; cranial nerves and special senses normal. Great weakness of both hands R. > L. Abdominal muscles so weak that he could not sit up in bed. Absolute paralysis of the right leg and almost absolute paralysis of the left leg. No wasting. Complete loss of sense of passive position in the lower extremities. Relative anæsthesia to all forms below the umbilicus. Sphincters normal.

Reflexes.—Knee, wrist, and elbow-jerks exaggerated; double foot clonus. Plantar reflexes brisk.

Skin of the feet thin and shiny. Temperature 98° F. to 100·5° F.

On the ninth day after admission the temperature rose to 103° F., and complete paralysis of the legs, complete incontinence and profound anæsthesia appeared. Two days later the knee-jerks were lost, and marked vaso-motor paralysis and œdema set in. He remained for a week in an apparently moribund state, with muttering delirium, and developed a right-sided pleurisy and a large sacral bedsore. At the end of this time he began to improve rapidly. The temperature fell. The anæsthesia and incontinence disappeared. The bedsore healed, and the spastic symptoms returned to slowly disappear in the course of the following two months.

At the time of writing this patient is at work, and the only sign of his illness that remains is the scar of the large bedsore.

During the acute stage of his illness he was treated with iodide of potassium and strychnine. During the last year he has had five epileptic attacks, never having previously had an attack.

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THE PATHOLOGICAL FINDINGS IN A CASE OF GENERAL CUTANEOUS AND SENSORY ANÆSTHESIA WITHOUT PSYCHICAL IMPLICATION.

BY HENRY J. BERKLEY.

Clinical Professor of Psychiatry, The Johns Hopkins University, Baltimore.

THE detailed clinical history of this case can be found in BRAIN (vol. xiv., 1891, part iv., page 44). A careful search of the medical literature has disclosed no similar instance occurring either before or since the date of its publication.

A synopsis of the clinical record as then published shows:—(1) A strong hereditary tendency to nervous instability, the mother, two maternal uncles, two brothers and two sisters having been insane. The father had died of tuberculosis. (2) A syphilitic infection acquired from her husband at the age of 29 years, subsequent to which the patient had several abortions, sore throat and falling out of the hair.

For twenty-two years, after the subsidence of acute symptoms due to the syphilitic process, there was fair health. Then came an attack of acute arthritis, after which the patient never fully recovered her former physical condition. Within a few months thereafter her eyesight began to grow dim, there were sudden flashes of light before the eyes, and vision was gradually extinguished, only sufficient remaining to enable her to distinguish light from darkness.

In the early summer of 1889 (nearly six years after the rheumatic attack) the patient began to experience a general tingling and formication in the skin of the entire body, which was shortly followed by several spells of uncontrollable vomiting.

A consensus of the numerous examinations made during the years 1889 and 1890 showed a total loss of thermic, pain, olfactory, gustatory, equilibrium, pressure and weight sensations; almost total loss of the visual sense, and a partial loss of tactile and muscular impressions, muscular sense and auditory perceptions. None of the special senses or cutaneous sensations remained wholly uninvolved.

Besides these disturbances of the sensory apparatus, several other symptoms of almost equal prominence were recorded.

The musculature, while responding to the will, did so in such a feeble manner that the patient was incapacitated from helping herself to any extent. Thus the dynamometer, when taken in the hand and squeezed, was so feebly compressed that the indicator showed no movement of the dial, though the woman exerted every effort in the trial. Despite this fact, however, both nerves and muscles responded promptly to the galvanic and faradic currents, nor was there anything abnormal noticeable about the quality or time of the reactions.

The cutaneous reflexes were all abolished. The faucial and pharyngeal reflex movements were absent, and a sound could be passed over the epiglottis into the larynx without eliciting a sensation of discomfort or inducing cough. During the attacks of vomiting there was no sensation of nausea.

When first examined the knee-jerks were present and normal. The biceps-jerk could also be elicited with some little trouble. The reaction of the abdominal muscles was lost, and the ankle beat was feeble. By the middle of July, 1890, the right knee reflex had disappeared, and the left one was weak. All other reflexes, deep and cutaneous, had been completely abolished. A year later the jerk of the left patella tendon was found to be extinguished.

Furthermore, with auditory perceptions a progressive dulling could be noted. When the woman was first admitted to the hospital the sense of hearing was fairly acute in both ears. Gradually the difficulty in receiving auditory impressions increased, until finally the voice could not be heard except with strenuous effort.

The ophthalmoscopic examination showed an extensive choroiditis pigmentosa, with atrophy of the optic nerves. Only a few vessels could be seen in the retina, and these were of minute size. In both lenses there was a beginning cataract.

Whether the optic nerve atrophy should be considered part of the general disease-process, beginning as it did long before the other symptoms, is somewhat problematical, though in tabes the same trouble is not infrequently noted as a forerunner of definite symptoms of the disease.

The pupils were at first in a state of mid-dilatation, and responded slowly to light, direct or reflected. They did not dilate on irritation of the cervical sympathetic. At a later stage the pupils became somewhat narrower, but remained sluggish to stimuli.

There were a number of interesting disturbances of the glandular secretions. During the fall of 1889 the mouth was found to be almost absolutely dry, the tongue heavily cracked, the epithelium eroded from its tip and sides, while the entire buccal surface was red and congested. At the same time the secretions of the lachrymal glands had almost ceased, the surfaces of the conjunctivæ being dry and injected. The skin was also dry and devoid of odour. After a course of potassium iodide these phenomena slowly abated, and the secretions returned to a more normal state.

Various unusual sensations troubled the patient at times. Cramps of the gastrocnemii, sensations of burning between the scapulæ, a girdle feeling around the abdomen, and neuralgic twinges in the nerves of the extremities were often complained of. Occasionally there were chronic fibrillary spasms of the small muscles of the thumbs.

Attacks of diarrhœa, refractory to treatment with drugs, though yielding to a continued milk diet, occurred in the latter part of the winter of 1890. These were, on several occasions, followed by a protracted vomiting, without pain or nausea.

Trophic symptoms in the form of a bulbous appearance of the finger tips and ridging of the nails, together with purpuric spots, developed late in 1891.

Throughout the long course of the illness there was never the slightest departure from normal mentality on the part of the patient; no hysterical attacks, no pathological depression or exaltation, and no delusions or hallucinations were ever noted. A slight apathy was the only perceptible change in the mental phenomena, but this was not greater than is frequently noticed in those who have become blind and helpless.

In discussing the etiology of the sensory phenomena in the previous article, three possibilities were suggested. (1) That the malady was functional, an opinion largely influenced by the pathological findings in the three autopsies on cases of general cutaneous and sensory anæsthesia reported by von Ziemssen, Krukenburg and Schüppel, respectively. This view was held to be hardly consistent with the presence of an optic neuritis, loss of the reflexes and the trophic manifestations. (2) That the case was an obscure instance of syringomyelia, or (3) that the terminal end-apparatus of the peripheral nerve fibres was diseased.

Though many points are not cleared up by the autopsy and the subsequent microscopic examination of the tissues, the results obtained are sufficient to show that none of these explanations would hold good, the nearest approach to a correct diagnosis being found in the last conjecture—disturbance of the peripheral nervous system.

The patient's condition did not materially alter after the record of the case was published. The anæsthetic and other symptoms, from the reports of the house physicians to the hospital, remained about stationary, and, on the rare occasions on which I saw her, there were no additional phenomena to be noted other than a steady though slow decline of the vital powers. Late in the year 1893 another ophthalmoscopic examination was made by Dr. H. Friedenwald, who found in the left eye an extensive and typical retinitis pigmentosa, the papilla being blurred and of a dirty yellow colour. Few vessels could be noted. In the right eye the clouding of the lens was so profound that the retina could not be seen.

About the middle of May, 1898, Mrs. R. became slightly lethargic, a condition that slowly increased to coma, in which state she died on the 25th of the month.

The *autopsy* was performed ten hours after death, the body being still warm to the hand. The cadaver was not emaciated, and *post-mortem* lividity was visible only on the dependent parts of the back. Both pupils were strongly contracted, though the right was much smaller than the left, being a mere pin point opening. There were no iritic adhesions. The nails were ridged longitudinally. Rigor mortis was present in the extremities. No local atrophy of the muscles could be noted.

The cranial cavity was first opened. The bones were dense in texture, and somewhat thickened, measuring 10 mm. in the frontal, and 8 mm. in the occipital regions. No diploë were seen anywhere within the cut bones. The marking of the blood-vessels on the inner surface of the parietalia was quite deep. The dura was slightly adherent to the bones along the vertex. The Pacchionian granulations were enlarged and quite granular. The longitudinal sinus contained a small quantity of dark fluid blood, but no clots. The lateral sinuses were empty of blood. The dura mater was not thickened, nor adherent in any way, except for the slight adhesions already mentioned. About 50 c.c. of slightly blood-stained serum escaped when the sub-dural space was opened.

The pia mater was moderately thickened, the meshes being filled with a straw-coloured gelatinous material. Its veins were filled with dark fluid blood. Along the border of these vessels lay broad white lines marking the distension of the lymph spaces. This distension of the lymph channels did not extend along the arteries at the base. The thickening of the pia was greater in the parietal than in the frontal and occipital regions. In the right sulcus of Rolando there was a much heavier deposit of the gelatinous substance than on the opposite side.

The cranial bones of the vault were normally symmetrical, those of the basis cranii a little contracted.

Basal Vessels.

The vertebrals were normal in calibre, but each of them showed, 27 mm. below their union into the basilar, a small aneurismal dilatation. The posterior cerebellar arteries diverged from the parent stem at the usual place of departure and were normal in calibre. The middle cerebellar on the left side was normal in position and size, while the one on the right side was rudimentary. The anterior cerebellar arteries were normal in calibre and disposition. The posterior communicating arteries of the circle of Willis had a calibre only sufficient to admit a fine pin. The Sylvians were normal both as to their size and the distribution of the main branches. Both anterior communicating, as well as the anterior cerebrals, were of fair size. Scattered over the basilar, the anterior communicating, and Sylvian arteries, were a number of atheromatous patches of moderate diameter, but the arterial stems showed but little thickening, the majority collapsing when cut across.

The encephalon, inclusive of the soft meninges, weighed 1095 grammes. The thickened and vascular pia stripped off without detaching any bits of the cortical substance. But few of the larger arteries of the pia showed the presence of marked atheromatous changes.

Left Hemisphere.

The sulci and gray matter were of normal depth and fair development. The five primary fissures were typical in configuration. The pre-central fissure was bridged in two places by unusually broad bands of cortical substance. The convolutions of this hemisphere were small, rather intricate, but corresponded to the usual types.

Right Hemisphere.

The convolutions and fissures of this hemisphere were symmetrical with those of the left side, except that the anterior central convolution was much broader. The right optic nerve, on measurement, was slightly smaller than the left, though the difference was trivial. To the eye these nerve tracts afforded no evidence of gray degeneration.

On section of the hemispheres, the ganglia, the corpus callosum and the other inter-hemispheric bands, as well as the white matter, disclosed no evidence of disease. The choroid plexuses contained a number of small cysts.

The cerebellum weighed 140 grammes. There were no pathological changes to be discovered in it.

Macroscopic examination of the medulla and pons Varolii was distinctly negative in respect to naked eye lesions. The membranes around the medulla were a little thickened. The pyramids in the medulla were symmetrical.

The entire cord with the membranes and filum terminale were removed, but none of these structures showed any vestige of a diseased condition.

Thoracic Cavity.

The strands and ganglia of the cervical sympathetic nerves were in every respect natural. The lungs were normal. The pericardium contained a minimal amount of fluid. The heart weighed 250 grammes. The posterior segment of the mitral valve was much thickened. The intimal surface of the aorta was studded with deposits of calcareous material, but the vessel showed little general thickening. The aortic valves were normal.

Abdominal Cavity.

The liver weighed 980 grammes, but was structurally normal. Each kidney weighed 100 grammes. The capsules were strongly adherent to the cortical substance, and when peeled off brought with them portion of the subjacent tissue. The cortex was reduced in thickness, and the entire renal tissue was hard and resistant to the knife. The capsule over one-half of the spleen was enormously thickened, while over the other portion it was natural. The medullary tissue was normal. Pancreas, intestines, lymph glands and bladder, showed no evidence of disease.

A large number of pieces of the brain from the several regions were preserved in alcohol, formol, Müller's fluid and Flemming's solution. The entire cord was hardened in Müller's fluid and alcohol. Several bits of skin from the neck and abdominal walls were likewise preserved in alcohol and Müller.

The spinal cord under the microscope showed the most definite alterations, and accordingly will be first described.

Lumbar Cord.

Weigert hæmatoxylin.—The nerve-bundles of the filum terminale show no lesion. Throughout the whole of the lumbar enlargement the white columns have every appearance of health, the axis cylinders being distinct, the myeline abundant, and not at all varicose. In the gray tracts, the finer fibres inclusive of the commissural are well stained and show no indication of degeneration. Neither the anterior nor posterior root fibres have any signs of pathological change, although there is considerable thickening of the pia around them. The cells of the anterior horns are fairly numerous. Some of them contain heavy depôts of pigment granules, while others are entirely free from the metaplastic material.

Dorsal Cord.

The lowermost portion of this segment is equally free from signs of disease in the medullated tracts, except that the posterior commissural fibres are not so numerous as in the lumbar regions. When, however, the level of the ninth dorsal vertebra was reached, a small area of degenerated fibres first becomes visible in the right column of Burdach, in close proximity to the Goll column. This area is very small. It is at first entirely separated from the pia, but soon approaches it more closely, and finally touches the free margin. The form of the degenerated tract is irregularly pyramidal in shape, the base broad lying upon the external margin, the apex, sharply defined from the undegenerated tissue, penetrating more deeply. This degenerated area contains few normal fibres, and none at all in the central and apical portions. They become more abundant as the margin of the column is reached. The majority of the nerve-tubes within the altered tract are much atrophied, with here and there an enlarged and varicose axis-cylinder among them. The root fibres at this level of the cord show no distinctly degenerated tubes, but contain more than the usual number of fine fibres that take the Weigert stain imperfectly. All medullated tracts within the substance of the cord are definitely normal, except that the bundles composing the posterior commissure are scanty.

A few millimetres above the beginning of the degeneration in the posterior column (at the lowermost border of the seventh dorsal vertebra), a new area of degeneration is seen,

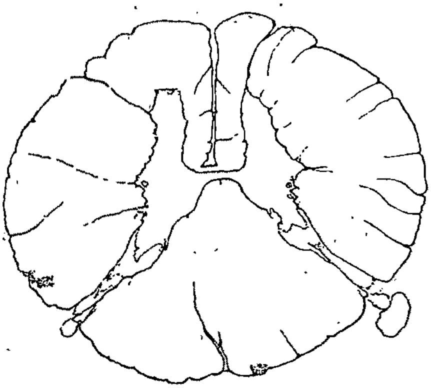

FIG. 1.

Outline drawing of a transverse section of the upper portion of the dorsal cord, showing the location of the degenerated areas in the posterior and postero-lateral columns.

this time in the left postero-lateral column. At first it appears, under a magnification of 80 diameters, as a circular patch not larger than the head of a pin lying close to the Lissauer zone, though not within the indirect pyramidal tract, and well separated from the external border of the cord. Very shortly it enlarges and assumes a wedge-shaped appearance, having its broad base on the external border of the cord and its apex toward the deeper regions, and lies within the direct cerebellar fasciculus. This area contains a scattered number of apparently normal fibres interspersed among the sclerotic ones.

The root fibres, both anterior and posterior, show the same general conditions as those a few centimetres lower, nor do the posterior fibres that have entered the root zones, with a few exceptions, exhibit other than normal conditions. The interior medullated tracts, except those already mentioned as degenerated, the finer fibres of the gray horns, the commissural fibres, are all apparently sound. The posterior commissural fibres are again deficient in numbers.

Lowermost Cervical Cord.

The appearance of the degenerated tracts is the same as in the higher dorsal levels. As higher regions are reached the degenerated area in the right Burdach column soon begins to alter in size, and eventually entirely disappears before the beginning of the cervical enlargement is reached.

The sclerotic area in the left postero-lateral column on the other band constantly broadens, and at the same time

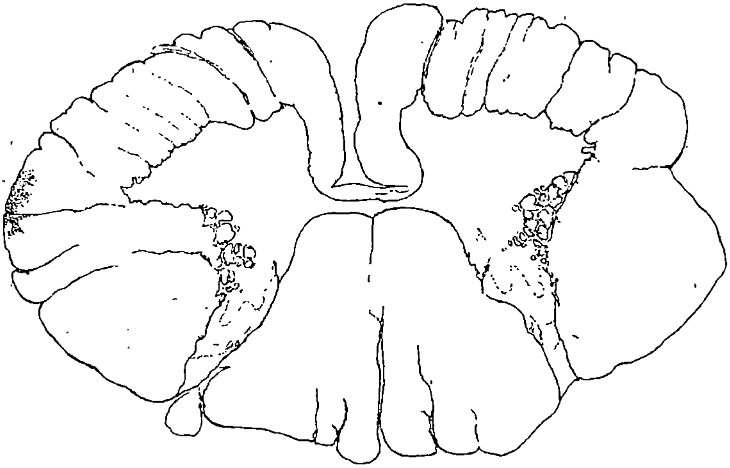

FIG. 2.

Outline drawing of a transverse section of the cervical cord above the middle of the enlargement, showing the changed position of the lateral sclerotic area.

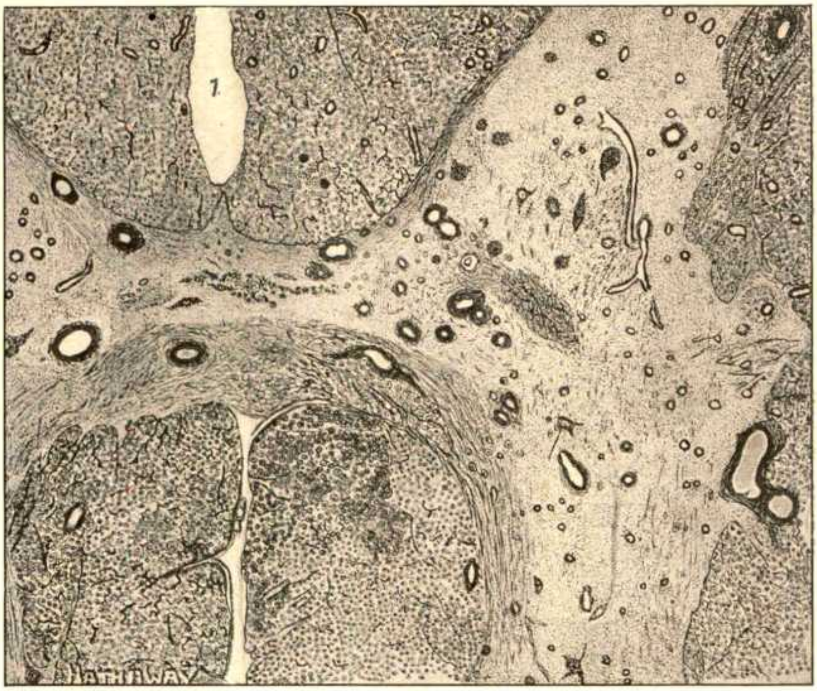

FIG. 3.

Transverse section of the dorsal cord, showing numerous thickened vessels in the neighbourhood of the commissure and adjacent gray matter. Enlarged about forty diameters.

moves from the posterior regions of the column to a position almost in the middle of the lateral region, occupying a place along the posterior edge of the Gowers' tract. Normal medullated fibres within its borders are few, the whole area being filled by dense sclerotic tissue. The wedge shape of the sclerotic zone is retained throughout this level, the borders of the degenerated being sharply defined from the normal tissue.

Cervical Enlargement.

The single area of degeneration at this level exhibits no deviation in size or appearance from that described for the lower cervical region, nor do the other columns, root-fibres, or fine bundles and single fibres of the gray matter show any departure from the normal, beyond that again the posterior commissure has almost no fibres in it.

In the uppermost portion of the cervical cord the degenerated tract spreads out a little towards its anterior boundary, and at the same time comes more directly into the Gowers' column; then at the level of the pyramidal decussation it becomes smaller, and is at length reduced to a narrow band along the anterior border of the cord, completely within this tract. The sclerotic area now rapidly decreases in size, and finally becomes lost at the level of the uppermost portion of the decussation; no degenerated fibres being evident in the direct cerebellar tract, or extending in the direction of the nucleus lateralis. The cells of this nucleus are numerous, not atrophied in the least, and do not differ in any way from those in the adjacent nuclei of origin.

Sections were made through the pons up to the level of the exit of the fifth pair, but without discovering any further traces of degenerated fibres. All the roots of the cranial nerves, with one exception, contained apparently healthy fibres. This was in a small bundle running in the right eleventh nerve, in which there was a considerable increase of connective tissue fibrillæ and a few degenerated medullary fibres, in all probability owing to the closure, from hypertrophy of its tunics of the lumen of a local artery passing through the nerve bundle.

The Marchi preparations, for some unknown reason, did not take the stain perfectly, and all that could be determined from them was that a few isolated nerve-fibres of the posterior roots, both internal and external to the substance of the cord, as well as a few fibres of the anterior roots, took the black colour.

The Optic Nerves.

Weigert hæmatoxylin.—The blue-black staining of the myelin was hardly taken at all by the sections of these nerves. To provide against errors, other sections were again stained by the same procedure, but the result was identical. Faint bluish lines are here and there seen in the nerve-bundles, with now and then a more distinctly stained tube scattered among them. Between the atrophying nerve-fibre bundles thick masses of a coarse fibrillated connective tissue have penetrated, which are tinged a brownish shade by the hæmatoxylin. Between the individual nerve-fibres are finer strands of connective tissue elements, derived from the thicker bundles. Both optic nerves are equally affected in the degeneration, and but few nerve-fibres in either of them have escaped total destruction.

In the optic tracts the vessels, arteries and veins are everywhere greatly thickened, the muscular coat being altered as in the segments of the cord, and almost to an equal degree. The meninges around the optic nerves are not perceptibly hypertrophied or filled with nuclei, though they contain many diseased vessels.

Internal Capsule and Basal Ganglia.

Weigert-hæmatoxylin.—The nerve-fibres are distinct and well stained by the hæmatoxylin, and show neither diminution of their numbers nor atrophy of the myeline sheath, which is abundant and not varicose. The capillaries are distended with blood. The veins are dilated, but hold little blood. The arteries, for the most part, are nearly normal; here and there is one showing distinctly the lesions of the muscularis, to be presently described.

At the level of the exit of the fifth pair, and close to the ventricular margin, a number of hæmorrhages, extending beyond the extravascular sheath into the nerve tissues, were also found; but in these the corpuscles retained their form, and the vascular rupture had probably taken place just before death.

The Pia Mater Spinalis.

The soft membrane throughout the length of the cord is thickened, but much more in the lower dorsal region than above or below it. This hypertrophy of the membrane consists chiefly in a simple overgrowth of the connective tissue trabeculæ, without any nuclear proliferation. The arteries and veins contained in the pia are all immensely thickened, but this alteration varies considerably in its histological characters in different vessels. In the largest arteries—for example, in the arteria spinalis anterior—the intima is approximately normal, while the muscular lamina is greatly thickened. In this latter layer the nuclei are too numerous, though for their kind perfect in form and staining; but among them those conforming in appearance to the usual nuclei of smooth muscle cells are seldom seen. The adventitia is not disturbed either in respect to its nuclei or the connective tissue fibres.

In a few large arteries running lengthwise in the cord's envelope, the endothelium and fenestrata have separated from the muscularis, probably a *post-mortem* change, while the latter layer has assumed a coarsely fibrous aspect, and holds but few nuclei of any kind. The fibres making up the former muscular layer are arranged in a wavy fashion, resembling to some extent the infoldings of a fenestrata, and on a superficial examination the whole layer might be mistaken for a multiplied elastica. That such is not the case is readily determined by the fact that a perfect lamina is often found internal to the fibrous layer.

In not a few of the moderate-sized arteries the lumen is closed completely, solely from the overgrowth of the middle layer. The fibrous tissue shows no evidence of hyaline degeneration with picric acid.

The contents of the lumen of such vessels as are not obliterated is not uninteresting. With eosin-hæmatoxylin, or the van Gieson stain, the whole canal is seen to be filled with a material containing no blood corpuscles and homogeneous except for a faint granulation. In preparations by other stains the homogeneous substance is found to contain a few epitheloid cells with a round nucleus.

The smaller arteries also present considerable variation in their structural conditions. A majority have their walls thickened in the same manner as in the larger vessels, while in others there is a minor but distinct degree of hyaline degeneration of the middle lamina; it now assuming a yellow-brown tint with picric acid fuchsin. When there is hyaline alteration, the nuclei are sparse and deformed. In a few arteries the elastica is reduplicated, or even quadruplicated, and at the same time the lumen is narrowed so as to be completely obliterated, or the small opening internal to the intima is filled with a mass of epitheloid cells, in which stainable nuclei are uncommon.

The walls of the veins are almost equally as thick as those of the arteries, but in the place of having the lumen narrowed it is dilated, and the outline is often irregular.

The root-fibres contain thickened vessels, some patulous, others obliterated. Numbers of the vessels among the root-fibres showed a considerable degree of hyaline degeneration. Nowhere do the nerve-bundles show any great augmentation of the connective tissue elements. The axis-cylinders are often fully stained by the aniline dyes used, and are apparently perfect.

At one point surrounding an artery coursing longitudinally in the meninges, just outside the posterior external field of the left Burdach column in the lower dorsal cord, lies a nodule of partially disintegrated round cells which bears much resemblance to a gummatous neoplasm, which, after growing to a certain extent, had degenerated. The extent of this new formation is small, only running through eight transverse sections of the cord. The lumen of the artery near its centre is patent. There is a moderate polynuclear leucocytosis noticeable in the contents of the vessels. The thickened pia is nowhere adherent to the cord.

Vessels within the Cord.

Aniline stains.—The veins contain an abundance of polynuclear leucocytes. The walls of the vessels are often immensely hypertrophied, some of those in the anterior horns measuring 0·25 to 0·12 mm., and are visible to the naked eye. Others in the medullated regions are equally large. There is everywhere hypertrophy of the walls, principally of the middle layer, and at times it is difficult to distinguish between artery and vein. The vessels appear to be unduly numerous everywhere; there is no actual new formation of vessels, but the smallest arterioles, even the capillaries, are so thickened as to be unduly prominent in the microscopic field. This is more especially true for the gray horns than medullary tracts. The horns seem to be strewn with vessels of all sizes, from those visible to the naked eye to thickened capillaries. The region containing the most numerous diseased vessels lies lateral, on both sides, to the gray commissure, and in Clarke's columns.

The diseased arteries and veins are all of one type. The intima is but slightly affected, a little thickening of the sub-endothelial tissue being now and then noted, resulting in some irregularity of the lumen; but it is upon the media that the greatest stress of the disease has fallen. This layer is greatly thickened, and presents either a fibrous or hyaline appearance, according to the duration and intensity of the disease-process, the hyaline apparently preceding the fibrous change. In some of the vessels the peculiarly-shaped nuclei of the muscular tissue are to be seen at infrequent intervals, distorted and shrunken to such an extent as to be hardly recognisable. In others no nuclei at all are to be found, and the lamina, though fibrous, is homogeneous in character. With the van Gieson stain, the media of a number of vessels takes on a red colouring, but this is diffuse over all the layers, and not confined to the middle one. In still others the stain acts differently. The intima and adventitia are tinged red, while the muscularis takes only the yellow of the picric acid, and appears not striated, but perfectly homogeneous.

Externally from the muscularis irregular lymph spaces are often noted, corresponding to local dilatations of the intravascular space. These sometimes contain a few leucocytes. In the adventitia around these vessels there is little or no morbid changes. It is not unduly thick or fibrous in character, and contains a moderate number of round and oval nuclei.

Eosin-hæmatoxylin preparations show essentially the same pictures of the morbid process in the vessels as the picro-fuchsin stain. The intimal alteration, however, comes out more clearly. There is distinct though slight hypertrophy of the layer, with multiplication to a limited degree of the endothelial cells. The lumina are nowhere closed, though there may be great thickening of the media. Its ring-like appearance is also rarely disturbed.

The lesions of the arterial system, while diffused throughout the entire length of the cord, are much more pronounced in the dorsal region than elsewhere, and especially in the lower portion of this tract. Accordingly, in the lumbar and cervical levels there is, by comparison, but little thickening and disease of the veins and arteries, though, in truth, the degree is very considerable.

In the extravascular spaces, especially along the edges of the adventitial layer of the vessels, there are frequent depôts of hæmatoidin *débris*, as well as a finely granular material, that takes up considerable quantities of the aniline dyes.

The walls of the vessels in the *medulla* and *pons* show in individual instances a considerable thickening, on the same order as in the dorsal cord. But while all the vessels have some disease of their sheaths, in but few of them is the disease extensive. In two large arteries running longitudinally through the length of the medulla, just beneath the floor of the ventricle and in close proximity to the median line, an extensive hyaline thickening was noted, and around them, filling up the perivascular space, are quantities of fresh red and white blood corpuscles.

In the *cortex* and *ganglia* of the brain, arterial lesions are not profound, though here and there a vessel considerably thickened may be noted, the degeneration affecting principally the middle layer.

In the *meninges* of the brain and bulb fairly numerous thickened arteries are to be found. These are not equally distributed, but only occur now and then. The points of selection in the region of the pons and medulla for the pronouncedly altered vessels are either around the nerve-roots or between the nerve-bundles. In almost any of the cranial nerves several of these pathological vessels may be seen, but it is only now and then that a degenerated and atrophied nerve-tube is noticed in the bundle.

Arteries of the Thoracic and Abdominal Skin.

The general histology of the integument seems to have suffered no essential change, though the blood-vessels are everywhere considerably thickened. In some the morbid alteration is much greater than in others, and hyaline changes in the media are noticeable. When this occurs there is complete disappearance of the muscular elements and their nuclei. The endothelial and sub-endothelial structures are also slightly hypertrophied. The nerve-bundles—so far as could be determined with the fuchsin stain used—presented no departures from the normal.

Nerve-cell Bodies.

Alcohol hardening and hæmatoxylin-eosin stain.—The nerve-cells of the anterior horns show about the same condition on the two sides. There is an advanced metaplastic change in the substance of the elements, but this is hardly beyond what one might be led to expect from the moderately advanced age of the individual. The Nissl-bodies in the non-pigmented portions are distinct and rather coarse in appearance, and are arranged somewhat irregularly in the cytoplasm.

The nucleus is sometimes very distinct, sometimes of normal outline and contents, while at others it is indistinct. A few of them are stained very deeply, and the contour is irregular and roughened. The nucleolus in the majority of the well-defined vesicles is not altered in outline, but accepts acid stains in preference to the basic hæmatoxylin and other dyes, standing out as a bright red spot in the centre of the nucleus. The position of the nucleus is usually central.

In the columns of Clarke the pigmentary changes in the nerve-cells are greater than elsewhere, and attain a pathological degree; and, besides, there are a number of cells that have undergone simple atrophy, having shrunken to a small mass in one corner of the peri-cellular space. These atrophic cells are more numerous in the lower dorsal region of the cord than in the lumbar, upper dorsal, or cervical regions. The small nerve-cells in the posterior horns by this method of staining show no definite alteration. The cells in the lateral regions of the gray horns have few departures from the normal.

Safranin staining.—Many of the cells in all the anterior regions of the gray horns, but particularly in the columns of Clarke, are completely filled with coarse yellow pigment granules, among which a shrunken nucleus is now and then demonstrable. No nucleolus is visible in the atrophied vesicles. In rather infrequent instances the nucleus is pushed to the extremity of the cell.

In the cells that have no well-marked accumulation of pigment granules in them the Nissl-bodies are coarse, do not retain their usual arrangement, but are irregularly distributed through the protoplasmic substance. They also, at times, show a tendency to group together at the periphery of the cells, leaving a clear ring of considerable size around the vicinity of the nucleus. At other times there are scattered clumps of granula in the protoplasm. Among the better preserved cells are some that are shrunken to a small mass of finely molecular material in which neither nucleus nor nucleolus is visible.

The state of the nucleus varies considerably in the least damaged cells. In a majority caryoplasm and chromatin particles are normal, but there are also a variable number in each section in which the vesicle has the appearance of being swollen, and the caryoplasm is devoid of stainable substance. In a very few instances there is a double nucleolus marking the presence of an irritative process.

The Nissl methylene blue stain gives identically the same results as the safranin.

Upper Cervical Enlargement.

Safranin alcohol stain.—The cellular state is identical with that at lower levels. Nowhere in the white columns of the cord, with the exception of the slightly sclerosed areas, was any morbid process to be noted in the neuroglia structures or in the medullary tubes.

Nissl methylene blue.—The irregular disposition of the granula is shown by this method with even greater clearness than by safranin and hæmatoxylin. The tendency is always to aggregate into clumps near the periphery of the cell body. A portion of the cells, however, show a normal arrangement. The large masses of yellow pigment grains stand out in striking contrast to the blue of the Nissl-bodies. Quite often the pigment covers the nucleus. In some cells, in contrast to those mentioned, the chromophilic substance is irregularly diffused throughout the cytoplasm, and in these the ordinary appearance of the Nissl granula is lost.

Quite a number of the cells show shrinkage and irregularity in the contours of the nucleus. The vesicle also has a tendency to retire to the periphery of the protoplasm. This disposition of the nucleus is more often apparent in certain regions of the gray columns of the cords than in others. Thus in the columns of Clarke it is common, while in the ventral portions of the lateral horns it is infrequent.

Medulla oblongata. Lower regions.

Deviations from the normal in the cell body are much less pronounced than in the dorsal cord. Among the cells in the scattered nuclei of origin on the floor of the ventricle there are here and there nerve elements that show displacement of their nuclei. These are irregular, distorted, and shrunken. The lesion of the nucleus is dependent, at least in part, on a simple atrophy of the nerve-cell as the result of an imperfect supply of nourishment. The protoplasm of the cell, accordingly, shows a diminution in its bulk, with corresponding enlargement of the perivascular space. Diseased cells on the whole are not common, and few of the nuclei of origin of the cranial nerves have any considerable numbers of them.

Middle and Upper Regions of the Medulla.

Van Gieson stain.—The nuclei of the nerve cells are much more frequently displaced than lower down in the bulb, and the membrane of the vesicle is shrunken and irregular. The bodies of the cells show atrophy. In the nuclei, in the region lateral to the central V-shaped point of the ventricle, there are numerous very heavily-pigmented cells. The pigment consists of the usual yellowish-brown grains, but the whole body of the cell is filled with it, and the intrinsic nucleus is no longer visible. Some of the nerve elements are evidently in process of disintegration, and when, as is occasionally the case, their nuclei can be seen, they are shrunken and distorted. Double nucleoli are by no means infrequent in these bodies, and changes in the receptivity to dyes are noticed. The morbid process is most marked in the nuclei of origin of the tenth, eleventh, and twelfth cranial pairs. Here, accordingly, there is a more advanced degree of arterial lesion than lower in the medulla.

Safranin staining.—Some of the nuclei of the cells have local thickenings of their membranes, but the caryoplasm and nucleoli are apparently normal. In others the nucleolus is doubled, or, when single, appears much roughened. Often the nucleus is forced to the extreme edge of the protoplasm, or even partly extrudes through its boundaries. The granular pigmentation of the cells is seen to be widely distributed, but only assumes distinct pathological proportions in the nuclei of origin, already detailed, and in the upper olivary bodies. In this last location the cells are filled to their utmost capacity with pigment and are disintegrating.

Eosin-hæmatoxylin slides give the same pictures as the safranin.

Nissl's methylene blue.—The superior portions of the olivary bodies have a pathological degree of pigmentation of their nerve cells. Elsewhere the accumulation of metaplastic material can hardly be said to be greater than is usual in persons of advanced years. In a considerable number of the olivary cells none of the blue stain is absorbed, and the granules of pigment are scattered loosely within the cell space, many of them lying apart from the main body. The Nissl granula are fairly well tinged in such cells as are not heavily pigmented. The cells of the glosso-pharyngeal nucleus have less pigmentation than any other nerve elements in this region.

Region of the Pons.

The nucleus acusticus dorsalis is heavily pigmented; all others have less of it than in the medulla. The nuclei of the cells of the acusticus are displaced, and the outlines of the vesicles are indistinct. The intra-medullary portions of the abducens nerves are normal; the axone and medullary covering being perfect in detail, as are likewise all other medullated tracts in the pons. The vessels are not profoundly diseased.

Cerebellum.

The larger arteries are thickened, but less so than in any other department of the nervous system previously studied. There is a slight hyaline degeneration of the walls of the vessels, but no visible implication of the inner and outer sheaths. The capillaries have apparently lost their elasticity, the walls are irregular and have numerous local bulgings. Their nuclei do not take the aniline stains well, and are shrunken.

The cerebellar leaflets do not appear to be atrophied in any way, the molecular and granular layers, with the cellular elements therein contained, being perfectly well defined. The neuroglia cells of the molecula lamina are not increased in number. The Purkinje cells take the aniline and hæmatoxylin stains in normal fashion, and their branches may be traced for considerable distances from the bodies. The Nissl granula contained in them do not depart in arrangement from the customary type. Few nuclei are otherwise than perfect, and these have only a slight thickening of the membrane. The nucleus, and chromatin of the caryoplasm are perfect. The nuclei of the basket cells of Kölliker show nothing abnormal. Within the granular layer the hæmatoxylin cells are well defined and exhibit nothing pathological. The white medullated cores show no morbid condition.

Cortex Cerebri. Vascular System.

In the small arteries of the soft meninges the usual indications of a hyaline degeneration of the middle coat may be almost universally noticed, but there is little or no thickening of the layer. The outer lamina is not at all involved, and in the intima there is but an occasional trace of thickening. Calcareous plaques are absent from the medium sized arteries. The veins are dilated to a moderate extent, and are filled with blood. Their sheaths present no evidence of a morbid process.

Within the layers of the cortex the degree of vascular disease is a variable one, but is nowhere profound; indeed, it is seldom more extensive than in the majority of persons who have reached the age of 70 years, though in this particular instance the morbid process is somewhat different in character. Nearly all the medium sized arteries show hyaline degeneration of the muscularis. This is not uniform, but is scattered in patches along the length of the vessel. In the local foci, where there is an advanced degree of the hyaline mutation, the muscularis is devoid of cells and nuclei, even the intima exhibiting shrinkage and distortion of the nuclei. In the intervals where a more normal character has been retained, the muscular nuclei are present but have slight atrophic alterations with vacuolarisation of the caryoplasm. The nuclei are fairly numerous, though they do not take up the aniline colours to any extent. A few of the vessels show some thickening of the adventitial layer, but fixed nuclear proliferation is scanty. In the greater number of the vessels the outer layer is not changed, beyond containing small quantities of hæmatoidin *débris.*

The smaller arteries and capillaries, like the larger ones, show a varying degree of disease. They are irregular in outline, their cut ends standing open as if they were ridged tubes, and for long distances their walls are devoid of nuclei. When a nucleus is seen it absorbs the aniline dye badly, and is shrunken and granular. A few vessels less seriously affected show only a moderate degree of deterioration of the nuclei, and accordingly a closer approach to a normal appearance. The larger veins are filled with blood to distension. Their sheaths are fairly well preserved, having the prevailing hyaline degeneration only at irregular places. The perivascular spaces are not dilated.

Occipital Region.

The changes in the vascular apparatus are identical with those in the convolutions bordering on the central furrows. A single miliary aneurism was discovered in the entire number of sections, and this was located in the sub-cortical white matter. One small artery stopped by a thrombotic plug was also noticed.

Nerve-cells of the Cortex.

The Nissl staining of the chromophilic bodies in the large pyramidal cells is more than fair, and the arrangement of the stainable substance is regular. The amount of yellow pigment in the pyramidal cells is not above the normal for a person that has nearly reached the natural limit of life, and is not diffuse, but confined to one corner of the cell body. The nuclei and nucleoli are natural in appearance. With the eosin-hæmatoxylin dye the cortical cells appear to be normal. The safranin dye brings out more distinctly the atrophic changes that are incidental to the involutive period of life, but the alterations are not profound.

The neuroglia does not show any increase in the number of nuclei except along the course of a few of the larger vessels in the sub-cortical medullary tracts.

Corpora Striata and Lenticular Nuclei.

The cells in these localities are slightly more pigmented than in the cortex, owing to the more extensive vascular degeneration. The neuroglia nuclei are not increased in numbers in other localities than around a few large vessels. In the *optic thalami* conditions are identical with those described for the corpora striata.

In the vessels of the ganglia the hyaline condition of the middle coat is very prominent. In a few locations there is in addition a well-marked proliferation of the nuclei of the adventitia. The extravascular spaces are wide, and a few of them are filled by a plastic exudate that stains a faint rose with eosin. No necrotic foci were found around any of the arteries.

To *recapitulate:* The fundamental pathological basis for the various nervous phenomena described in the clinical history of the case is as follows:—(1) A hyaline-fibrous degeneration of the arterial system existed, which was not confined to the central nervous regions, but was equally evident in the roots of the spinal nerves, and in the skin tissues. The degree of alteration varied from slight thickening of the muscular layer to complete closure of the lumen from hypertrophy of the middle coat of the vascular walls. The morbid change was accordingly not uniform, but reached its maximum of intensity in the vessels of the lower dorsal cord, the meninges of the bulb and cord, and also in certain of the root-bundles of the cerebro-spinal nerves. (2) As a consequence of the vascular lesions there were degenerations of an atrophic order in the nerve-cells of the gray horns of the cord, more particularly in those of Clarke's column, and in the medulla oblongata. To this alteration in the central nervous substance at least a portion of the various symptoms must be attributed.

Besides the principal lesions there were others of considerable, though minor, importance.

The degeneration of scattered fibres in the bundles of the spinal and bulbar nerves played some part in the general symptomatology, being shown during life by the lowering of tone as regards the innervation of the muscles, as well as by disturbances of the functions of the nerves extending from the terminal apparatus.

The sclerosis of a portion of the outer zone of Burdach's column would signify that fibres ascending through the posterior root zones were degenerated, though the small area involved determines that their numbers were inconsiderable. The lesion of the tract itself has but little significance, the fibres implicated belonging to short inter-connecting bands.

The lesion of the direct cerebellar tract is not only of more importance, but presents some rather peculiar features. The absence of the majority of the medullated fibres from the posterior commissure, over considerable regions of the medulla spinalis, favours the view that a portion of the cerebellar bundle is formed from the fibres of this commissure. The gradual change of position in the sclerotic area shows also that the fibres—at least in this instance—do not proceed directly upward in the column, but are gradually diverted as other fibres enter, and assume a more and more anterior position; and, furthermore, that a portion of the fibres are lost in the upper cervical and lower regions of the medulla, and do not proceed to higher levels. This ending of the ascending fibres has been ascertained for a part of Gowers' bundle, but is not usual in the case of the component medullated fibres of the direct cerebellar tract. At its beginning the degenerated area almost touched the left posterior root zone, while in the upper cervical region it verged upon, if it did not enter, the area assigned to Gowers' bundle.

The total disappearance of the degenerated area at the lowermost level of the medulla may be considered to have sufficient anatomical value upon which to base the theory that in the so-called direct cerebellar tract other fibre-bundles, which are at present unknown, enter into its formation, and that these correspond more closely in their manner of terminating to the bundles of the Gowers' system than to those of the cerebellar paths. The deportment of the sclerotic fasciculus may also give rise to the supposition that we have to do here with an undescribed bundle, running from the dorsal to the uppermost cervical region.

As an explanation of the numerous symptoms of the case it would appear most reasonable to suppose the existence of a disease-process affecting simultaneously both the peripheral and central nervous systems. Assuming that the arterial lesions were of late specific origin—and of this there can be but little reasonable doubt—a chronic progressive involvement of the nutrient channels, here and there leading to marked narrowing, or even to closure, of isolated vessels, might certainly have produced just such a train of symptoms as was present. Of primary importance would be the involvement of the arteries of the anterior and posterior nerve-roots of the bulbo-spinal system, though the direct lesions of the nutrient supply to the terminal nerve apparatus, which have to be inferred as they could not be definitely determined, would be of equal value. This inference of the implication of the end-apparatus is justifiable, since the arterial degeneration in the skin was quite extensive, and whenever there is starvation of a nerve tissue there result pathological reactions, which may be manifest in a multitude of ways.

The slowly progressive character of the symptoms is also consistent with the theory of tissue starvation. All the lesions of the nerve-cells of the cord and bulb are of this type—atrophy and pigmentary degeneration from mal-nutrition. When nutrition is at a low ebb, metaplastic granules accumulate in the protoplasm of the cell.

The condition of the optic tracts, in which the lesions are identical with those of other nerve-roots, except that they are more advanced, would argue that the thickening of the blood-vessels was of long standing, and that only when the process had advanced to an extreme degree did any definite symptoms show themselves. This is exemplified more particularly in the state of the cortex cerebri. Though in this region vascular disease was manifest and diffuse, it had not advanced nearly to such a degree as in the gray matter of the dorsal cord or in the adjacent meninges. As a consequence, the functions of the cortex, while not as perfect as in youth, were not reduced to the same low level as those of the cord and bulb.

One pathological fact should be remembered in considering the clinical symptoms, namely, that it is not necessary for a vascular lesion to proceed to such a profound degree as to cause the entire shutting off of the nutrient supply before a nerve-tissue will show signs of deviation from its normal functions. With a reduced supply of nutrient plasma definite manifestations of nervous exhaustion are brought about, and these are not due to a degeneration of the component portions of the neurone which is visible in the tissue after death, by our present methods of preparation, in the form of morbid alterations of the cytoplasm, axone or myeline. Long before this stage is reached the entire neurone is incapable of performing its natural functions in an efficient manner, and as a consequence anæsthesias, paræsthesias, diminution or exaltation of the reflexes, and dulling of the special senses may be noted. Almost precisely similar results are encountered in advanced stages of progressive paralysis, especially in the syphilitic cases, in which, when vascular lesions of the arteries of the cerebrum and cord have advanced to a profound degree, there is a gradual but progressive dulling of cutaneous sensibilities and special sensations.

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A CASE OF TRANSVERSE LESION OF THE SPINAL CORD, WITH A CONTRIBUTION TO THE LOCALISATION OF MUSCLES IN THE CORD.

BY PURVES STEWART, M.A., M.D., M.R.C.P.
Assistant Physician to the Westminster Hospital,

AND

WILLIAM TURNER, M.S., F.R.C.S.
Assistant Surgeon to the Westminster Hospital.

THE following case is of some importance, not only because of its symptomatology, which exemplified several interesting points, but also because the level of the injury was capable of demonstration during life by means of the X-rays and subsequently verified *post mortem* after an interval long enough to permit of the degenerations being traced with accuracy by the Marchi method. It thus affords a study of some value, both clinically and pathologically.

CLINICAL NOTES (by Dr. Purves Stewart).

The patient, K. T., a married woman, aged 28, was admitted to Westminster Hospital under Mr. Turner's charge on the morning of September 8, 1899, immediately after having fallen out of a window, a distance of about twenty-five feet. On admission she was found to be totally paralysed in the intercostal, spinal and abdominal muscles and in the lower limbs, and partially paralysed in the upper limbs, flexion and extension of the fingers being impossible. The temperature on admission was 95° F.

On examination of the patient on September 8, some twelve hours after the accident, the following observations were made:—

The patient is a well-nourished woman of good intelligence. Speech and articulation are normal. She is obviously paralysed, partially in the upper extremities, totally in the intercostal and abdominal muscles and in the lower extremities. There is moderate anæsthesia to touch and pain on the trunk below the third ribs in front and below the spines of the scapulæ behind; also along the inner borders of both upper limbs symmetrically from the axillæ to the fingers, the upper limit of the anæsthesia running along the long axis of the middle finger in each hand (*vide* fig. 1). At the level of the nipples in front and one inch below the inferior angles of the scapulæ behind, the anæsthesia and analgesia become absolute. No hyperæsthetic zone can be detected above the level of anæsthesia.

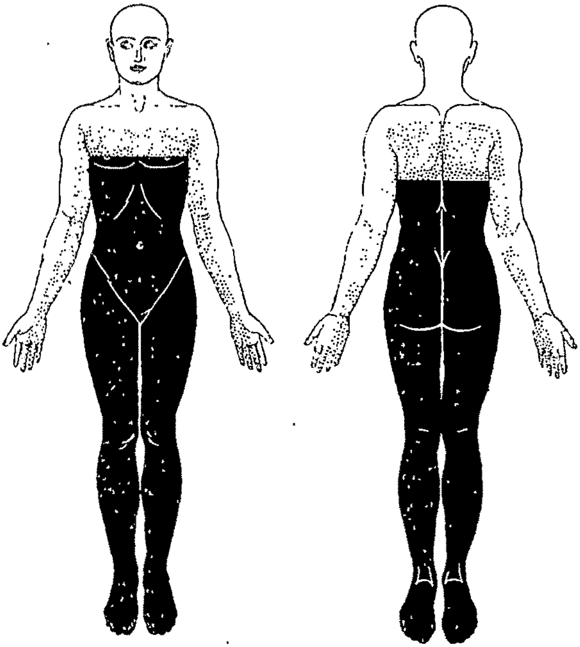

FIG. 1.
September 8.—Twelve hours after accident.

There is no evidence of paralysis of any of the cranial nerves. In the upper extremities the following muscles survive and can be voluntarily contracted on both sides, viz,, *biceps, deltoid, supinator longus, flexors of wrist, extensors of wrist,* and *upper part of pectoralis major.* The following muscles, on the other hand, are totally paralysed on both sides:—*Triceps, long flexors of fingers and thumb, long extensors of fingers and thumb, interossei, lumbricales, thenar,* and *hypothenar muscles, lower part of pectoralis major.*

The fingers and thumb are persistently semi-flexed at the interphalangeal joints in both hands; otherwise the posture of the limbs is not constant or stereotyped in any way.

There is total paralysis of the intercostals. The breathing is entirely diaphragmatic and quite easy. There is no dyspnœa and the extraordinary muscles of respiration at the root of the neck are not in action.

The abdominal and spinal muscles are totally paralysed; so also are the lower limbs, which are flaccidly extended at the hips, knees, and ankles.

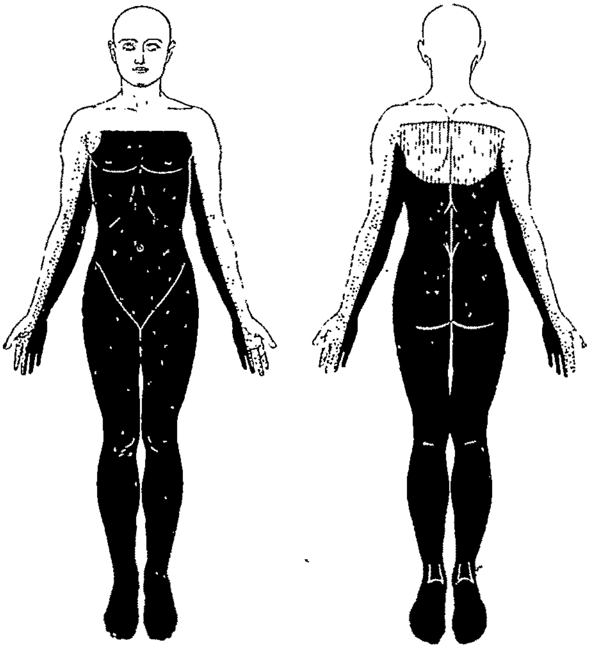

FIG. 2.

September 19—Twelve days after accident.

The knee-jerks cannot be elicited, although the vastus internus contracts to direct tapping on each side. There is no Achilles-jerk. The abdominal and epigastric reflexes are absent. The plantar reflexes are present and are extensor in type. There is absolute retention of urine, requiring the use of the catheter.

There is no tenderness in the region of the cervical spine, nor can any definite displacement of the vertebræ be detected posteriorly.

Temperature 99·4° F., pulse 84, respirations 24.

September 19 (twelve days after the accident).—The anæsthesia was again carefully observed (*vide* fig. 2), and the absolute anæsthesia was found to include the little and ring fingers and the ulnar side of the middle finger of the right hand, being less extensive on the left hand, where it only included the little finger and ulnar side of the ring finger. Slight impairment of sensation to touch, pain and temperature is somewhat more extensive than formerly, extending now as far as the web of the thumb on both sides. The upper limit of absolute anæsthesia on the trunk is still the same posteriorly, viz., below the angles of the scapulæ, but anteriorly it now extends up to the third ribs. No hyperæsthesia can be detected to light touches or pricks above the level of the anæsthesia; but the patient states that the skin in the region of the upper part of her chest feels tender when she is being washed.

The surviving muscles of the right upper extremity are stronger than in the left. Paralysis of triceps, flexors and extensors of fingers, and of intrinsic hand muscles is exactly as when she was admitted. To-day the *latissimus dorsi* was examined and was found to survive, contracting briskly on both sides when the patient coughed.

The pupils are moderate in size, equal and contract briskly to light and on convergence. They dilate sluggishly to shade.

The supinator-jerks are brisk; the knee-jerks are still absent. There is no ankle-clonus, but passive dorsiflexion of the ankle on either side produces a slow tonic contraction in the muscles of the calf. The abdominal and epigastric reflexes are still absent. The plantar reflexes both show an extensor response of the hallux. At the same time as the hallux becomes extended, the knee becomes flexed and the hip flexed and adducted. The superficial anal reflex is present on pricking the skin of the perineum. The deep anal sphincter, however, is paralysed and does not grasp the examining finger, and when the latter is withdrawn the anus remains for a time "yawning" widely open and after a few seconds it slowly closes. There is retention of urine with occasional "overflow" dribbling, which is kept in check by regular catheterisation.

All the muscles of the upper limbs, both paralysed and non-paralysed, were examined electrically with faradic shocks, and found to react normally.

An X-ray photograph of the cervical spine shows that the fifth cervical vertebra is dislocated forward on the sixth, the spinal canal being greatly narrowed at that level (*vide* plate).

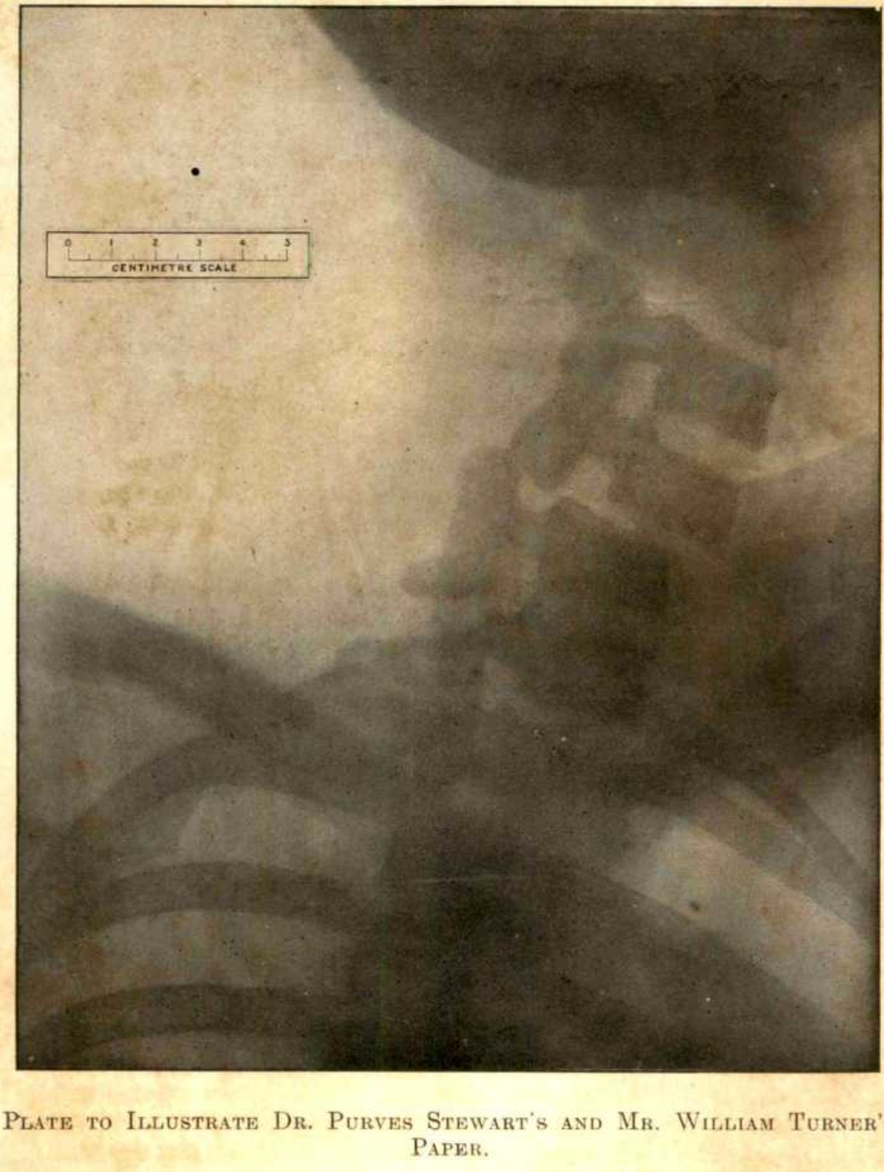

PLATE TO ILLUSTRATE DR. PURVES STEWART'S AND MR. WILLIAM TURNER'S PAPER.

September 20.—This morning, under an anæsthetic, Mr. Turner reduced the dislocation by extension. The displaced vertebra was felt to slip back into its place with a distinct jerk. Immediately before the operation the patient's knee-jerks were tested and were elicited for the first time since the accident, the left knee-jerk being extremely faint, the right a little less difficult to elicit. No Achilles-jerk on either side. Plantars still extensor in type. After the replacement of the dislocated vertebra an extension apparatus was applied with a weight of eight pounds to the head.

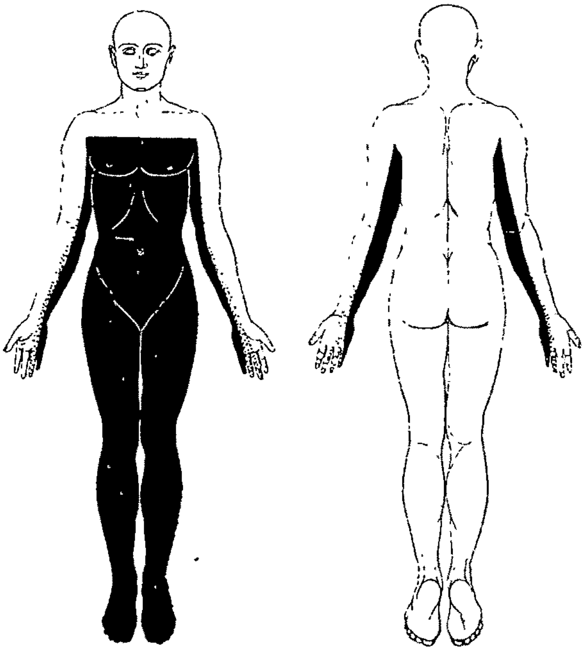

FIG. 3.

October 10.—*Permanent Anæsthesia.* A month after accident.

September 26.—Anæsthesia on front of chest same as when last noted. Upper limit on upper extremities splits the middle finger. Right arm distinctly stronger than left, though no previously paralysed muscles have yet recovered. Knee-jerks just present, the right being greater than the left, but both are very difficult to elicit.

October 10.—Surviving muscles exactly as before, including biceps, deltoid, supinator longus, latissimus dorsi, pronators, flexors and extensors of wrist and upper part of pectoralis major on both sides. The triceps, flexors and extensors of thumb and fingers, with all intrinsic hand muscles, are still totally paralysed. The fingers are semi-flexed at the interphalangeal joints; thumbs lightly adducted. The lower limbs are extended at the hips, knees, and ankles. There is distinct wasting of the intrinsic muscles of the hands and of the muscles arising from the internal condyle on both sides, but especially on the right side. The sense of position on passive movement is lost at all points of the little and ring fingers of both hands, being normal in all the other fingers and at the wrists, elbows and shoulders. Upper border of slight anæsthesia on the right hand reaches to web between middle and ring fingers; in the left hand it courses along the long axis of the middle finger (*vide* fig. 3). Owing to "extension" apparatus, limits of anæsthesia on back of trunk cannot now be tested. The tenderness of the skin of the upper part of the chest and root of neck, when patient is being washed, still persists. The supinator-jerk is present and brisk on both sides. The knee-jerks are just present, very faint, mere flickers. No ankle-jerk. Reflex incontinence of urine and fæces as before. Occasional flexor spasms of the lower limbs at hips and knees occur when patient is being moved in bed. Plantar reflexes to-day are both distinctly flexor in type. Healing bed-sores are present on both heels.

October 10.—Patient is discovered to be pregnant. The last catamenial period was about the middle of June.

October 11.—Temperature has gone up to 103·2° F. General bronchitis.

October 14.—Plantars to-day are both extensor in type. Knee-jerks can just be elicited, very faint on both sides. The temperature is up to-day (103°) and respirations are rapid, the chest wall being sucked in at each inspiration.

October 16.—Sense of position tested again to-day; lost in the two ulnar fingers of each hand. In the middle finger of the left hand, which is partially anæsthetic on one side only, the patient sometimes can tell the position of the joints correctly, but occasionally she makes a mistake. She is invariably correct with the middle finger of the right hand.

The pupils are equal in size and react to light. The right pupil was tested with a solution of cocaine and found to dilate well.

To-day, for the first time, she can make a feeble voluntary contraction in the triceps on both sides, but cannot extend either elbow against gravity.

Knee-jerks faint as before. Plantar reflexes both markedly extensor in type. The uterus is enlarged. The patient is apparently about four and a half months pregnant.

The faradic reactions of the arm muscles were tested and found to be as follows:—Normal reactions are present in the deltoid, biceps, supinator longus, and upper part of pectoralis major on both sides, also in the flexors and extensors of wrists (all these muscles can be voluntarily contracted). Normal faradic reactions also are present in the paralysed thenar and hypothenar muscles on both sides.

Diminished reaction to faradism exists in the triceps, lower part of pectoral and interossei on both sides; also in the flexors of the right fingers and the extensors of the right index and right thumb.

There is no reaction to faradism in the common extensors of the fingers or in the flexors of the thumb on either side, nor in the extensors of the left thumb or the flexors of the left fingers. The muscles of the lower limbs react briskly to faradism.

The bronchitis has now cleared up, and the temperature has fallen to 101° F.

October 30.—Patient examined by Dr. Rivers Pollock. Uterus just below umbilicus. Is about twenty-two weeks pregnant. Fœtal heart heard.

November 3.—To-day patient can extend both elbows feeble against gravity, the right better than the left. Pronation and supination are good on both sides; so also are flexion and dorsiflexion of both wrists. No movement whatever in the fingers of either hand. Atrophy of interossei, thenar, and hypothenar eminences and of muscles arising from the internal condyle on both sides. Both latissimi dorsi contract normally, also the clavicular head of pectoralis major on both sides.

Respirations are rapid, 42 per minute, and the trapezii and sterno-mastoids contract at each inspiration, whilst at the same time the anterior chest-wall becomes retracted. Copious rhonchi are heard all over the chest. Pulse 88, temperature normal.

Anæsthesia exactly the same as before. Tenderness of skin of shoulders and over manubrium sterni still present during washing. Loss of sense of position in two ulnar fingers of right hand and in three ulnar fingers on the left side.

The lower limbs are now semi-flexed at the hips and knees, with strong tonic adductor spasm. The knee-jerks are now brisk, but there is no ankle clonus. The plantar reflexes are extensor in type; the abdominal reflexes are absent. There is a deep bed-sore on the right gluteal region and superficial sores on both heels, although the patient has been on a water-bed ever since admission.

The pupils are equal in size (3 mm.); they react normally to light and dilate when shaded.

November 6.—General bronchitis. Temperature normal.

November 11.—Anæsthesia and motor paralysis as before. Knee-jerks brisk on both sides. No ankle clonus. Plantar reflexes extensor in type. Temperature 96·8°, pulse 94, respirations 33.

November 14.—Patient died at 6 a.m. from failure of respiration, which became somewhat accelerated (46) at the end, sixty-eight days after the original accident. Temperature at death 96·2° F.

Autopsy (eight hours after death).

When the body was turned on its face, the forward displacement of the fifth cervical vertebra was very evident, rendering the spines of the sixth and seventh vertebræ abnormally prominent.

The brain when removed showed no abnormality on naked-eye examination.

On opening the spinal canal no extra-dural hæmorrhage could be seen at any point. At the level of compression in the lower cervical region the dura was firmly adherent to the bones both in front and behind. At that level the theca was much flattened for a vertical extent of about 2½ cm., the flattened part being distinctly paler than the portions above or below.

On opening the spinal dura mater, the cord was found to be extremely thinned at the level of the upper part of the seventh cervical segment, being reduced to a mere ribbon with an antero-posterior diameter of only 1 mm. at its thinnest part.

The cord, medulla, and pons were placed in 10 per cent. formalin for microscopic examination. Sections were stained by the Marchi and Nissl methods and also with Delafield's hæmatoxylin and van Gieson's picric acid and fuchsin.

The degenerations found in the cord, medulla and pons are described by one of us in another paper.

There was no fracture whatever of the articular processes nor of any portion of either vertebra. The case was therefore one of pure dislocation.

The uterus reached to the umbilicus and contained a female fœtus apparently between the fifth and sixth month of gestation.

REMARKS BY MR. WILLIAM TURNER.

There is no doubt that this is a case of complete dislocation of the one vertebra on the other. This accident is comparatively rare as compared with fracture-dislocation, and is only possible in the neck. The inter-vertebral disc was broken, but the articular processes and laminæ of the vertebræ were quite uninjured. When the patient was first seen we could not diagnose any displacement, although it was very carefully looked for, and I fancy this must have been due to the partial slipping back of the bones into position again directly after the accident.

The spine of the fifth vertebra is always slightly depressed, and not so easy to feel as the others in the neck, and this, I think, makes the diagnosis of slight displacement more difficult still. The reasons why no operation was performed at first were that the condition of the patient showed quite definitely that the medulla of the spinal cord was at that time seriously injured, and this made the prognosis hopeless as regards cure from the first, and also the site of the injury. The operation at first contemplated was that of laminectomy. When, however, the fact was evident that dislocation had occurred, and that the position of the bones was far from satisfactory, we decided to try and reduce by means of extension in the hope that some good might perhaps accrue.

On admission she complained of some pain on the lower part of the neck, but there was no tenderness or prominence or depression in the region of any of the cervical spines. The seventh was quite distinct, and the others could be traced up in a middle line from it. There was no bruising in this region, and she had no pain radiating along the distribution of any of the nerve-roots.

The neck muscles were slightly more rigid than usual, and forcible movement of the head caused some pain, but this was quite indefinitely localised. Nine days after the accident it was noticed that the sixth cervical spine could be more distinctly felt than the fifth, and that it was on a distinctly posterior plane, and it was then decided that a skiagram should be taken from the side to confirm if possible the opinion that the condition was probably due to a dislocation or fracture-dislocation. The accompanying plate shows the result. It was taken by J. H. Montague, of 101, New Bond Street.

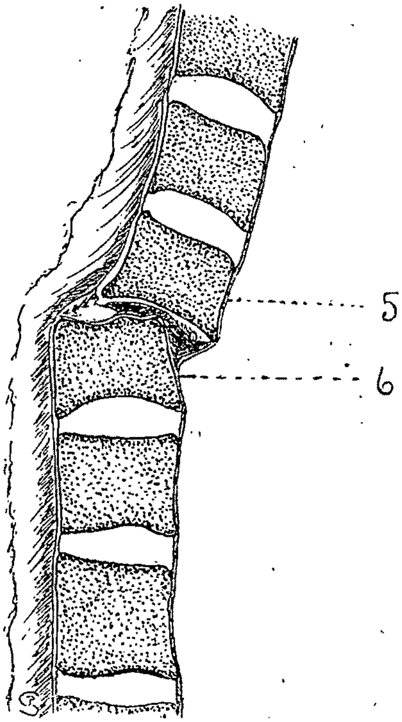

FIG. 4.

Vertical mesial section through dislocation (*natural size*).

The anæsthetic given was A.C.E., and the patient took it as easily as if she were quite well. Almost directly that I put extension on the head, standing at the head of the table, and with my thumbs on the transverse processes of the upper vertebræ, the bone slipped back into position with a distinct jerk, and did not appear to have any tendency to resume the abnormal position. A second photograph was taken by the X-rays two days after the operation, and showed that the displacement had been successfully reduced.

September 21.—The extension apparatus caused the patient a good deal of discomfort and pain in the neck, but not sufficient to discontinue its use. The level of the spinous processes is now normal. The weights extending the head were day by day gradually diminished, as the pain seemed to be more marked, and on October 16 only two pounds was used. It was then noticed that the position of the spinous processes was not quite so good as at the commencement of the extension treatment, and on November 10 there was no doubt that there was again some slight subluxation of the fifth vertebra on the sixth. This was verified on *post-mortem* examination, as may be seen from the drawing of a vertical mesial section through the bones.

REMARKS BY DR. PURVES STEWART.

The upward limit of the cord lesion, viz., in the upper part of the seventh cervical segment, was determined without much difficulty by the symptoms, motor and sensory. And this diagnosis was verified by the X-ray photographs, which showed with great clearness a displacement of the fifth vertebra forwards on the sixth, a vertebral dislocation which corresponds to a lesion in the cord between the sixth and seventh segments.

Another question was as to the amount of injury to the cord, whether total or partial. The complete paralysis of motion and sensation indicated that both the motor and the sensory paths were interrupted, whilst the wasting of muscles at the level of the lesion and their changed electrical reactions showed that the anterior cornual cells were destroyed at the site of the lesion. The absence of the knee-jerks during the first fortnight after the injury led one at the outset to suppose that the lesion was a complete transverse one. Fourteen days after the injury, however, the knee-jerks reappeared, though excessively faint, and thus led one for the first time to think that, according to Bastian's dictum,[1] there must still be some slight connection between the parts of the cord above and below the lesion. Such afterwards proved to be the case, although the band of uniting tissue measured only 1 mm. in antero-posterior thickness.

From the fourteenth until the fortieth day the knee-jerks remained excessively faint, so much so that Dr. Hughlings Jackson, who kindly saw the patient on the fortieth day, considered that, being mere flickers, they might practically be taken as absent. On the forty-seventh day, however, the knee-jerks became normal in excitability, and remained so until the patient's death on the sixty-eighth day. At no time were the knee-jerks exaggerated, nor could ankle clonus be obtained at any time.

The absence of knee-jerks for fourteen days, their reappearance and gradual return to normal without the development of ankle clonus up to the time of death, are all very instructive. Sir William Gowers, in the latest edition of his text-book,[2] still maintains, in opposition to Dr. Bastian and others, that after an acute lesion of the cord the knee-jerks may be abolished, but only for a few hours, in consequence of "inhibitory shock," but that if the lumbar centres are intact, they soon return.

In the above case, however, whilst the knee-jerks were absent for two weeks, the plantar reflexes were always elicited with ease, and it is difficult to assume that "inhibitory shock" should abolish the deep reflexes whilst the superficial reflexes survive. Two weeks seems an unusually long time for mere "shock" to cause absence of reflexes. Moreover, the constant presence of the plantar reflexes shows that the spinal centres below the lesion were still capable of excitation. Sir W. Gowers's further contention that absence of the knee-jerks for more than a few hours indicates a "parenchymatous inflammation," or descending myelitis, is not supported by our case. No such inflammation was found in the dorsal or lumbar regions, and the cells of the gray matter in those regions, on examination by the Nissl method, showed no abnormality.

The plantar reflexes were examined within a few hours after the injury and showed marked extension of the hallux instead of the normal flexor response. At no time were the plantar reflexes absent. This is in complete accordance with the observations of Babinski,[3] subsequently corroborated by van Gehuchten,[4] Collier,[5] and many others. On the nineteenth day, however, both plantar reflexes were distinctly flexor in type, but ever afterwards they invariably gave an extensor response. The significance of the exception is not clear. It shows, however, that whilst in lesions of the pyramidal tract it is the rule to have an extensor plantar reflex, yet exceptionally a flexor response may be temporarily present. The abdominal reflexes could never be elicited at any time during the accident.

The superficial anal reflex, got by pricking the skin of the perineum, was investigated on the twelfth day after the injury and found to be quite brisk, whilst the internal anal sphincter was quite lax and did not grasp the examining finger. Evidently the internal anal reflex is not to be classed physiologically along with the superficial anal reflex, since the former (non-striped muscle) may be paralysed, whilst the latter (striped muscle) survives. I have seen a similar loss of the internal anal reflex with preservation of the superficial anal reflex in a case of acute dorsal myelitis with flaccid paralysis of the lower limbs, the knee-jerks remaining normal; and, again, in a case of tabes with anæsthesia of the lumbar and sacral roots. I am not aware that this "dissociated paralysis" of the internal anal sphincter has hitherto been pointed out.

The last reflex to which we shall refer is the cilio-spinal reflex. Although the lesion was above the point of emergence of the rami communicantes to the cervical sympathetic, yet the sympathetic on the thirty-seventh day still retained its excitability to cocaine. Evidently, therefore, no degeneration had occurred in the pupil-dilating fibres of the sympathetic. The only explanation which seems to offer itself, is that the pupil-dilating fibres traversed the narrow band of tissue uniting the upper and lower portions of the cord without interruption, for, as we see, the lesion was not anatomically quite a complete one.

The muscular paralysis in this case is of special importance from the point of spinal localisation. The focal lesion was one of the seventh cervical segment, and the anterior roots of the seventh segment were the only ones which were afterwards found to be degenerated. Any muscles, therefore, which retained their voluntary motor power with unaltered electrical excitability must be innervated from segments of the cord above the seventh cervical, whilst of the muscles that remained paralysed, those whose faradic excitability was lost or diminished must be innervated from the destroyed seventh segment, and those with normal faradic excitability must be innervated from the eighth cervical or from segments below it. It must also be borne in mind that some muscles are represented in more than one segment of the cord, their motor nuclei in the anterior cornua having a considerable vertical extent.

The following table of muscles, classified on the above principles, is instructive:—

Deltoid	Not paralysed, and with normal faradic reactions	*Above* seventh cervical segment
Supinator Longus		
Biceps		
Pronators		
Supinators		
Clavicular part of Pectoralis Major		
Latissimus Dorsi		
Extensors of Wrist		
Flexors of Wrist		
Triceps	At first paralysed, afterwards recovered some motor power. Diminished faradic reactions	Seventh cervical segment
Common Extensors of Fingers (both sides)	Totally paralysed, with loss of faradic excitability	
Flexors of Thumbs (both sides)		
Extensor Indicis, L.		
Flexors of Fingers, L.		
Extensors of Thumb, L.		
Extensor Indicis, R.	Totally paralysed, with diminution of faradic excitability	*Below* seventh cervical segment
Flexors of Fingers, R.		
Extensors of Thumb, R.		
Sternal part of Pectoralis Major (both sides)		
Interossei (both sides)		
Thenar Muscles	Totally paralysed, with normal faradic excitability	
Hypothenar Muscles		

Of the above list of muscles there is already considerable evidence to show that the deltoid, supinator longus and biceps (together with the rhomboids and supra- and infraspinatus) are innervated chiefly from the fifth cervical segment. The present case has no bearing upon the distribution of the fifth segment, but so far as the sixth and seventh segments are concerned, several important points may be deduced.

According to the present views of most writers on this subject, the extensors of the wrist are to be grouped along with the extensors of the fingers at a common level situated one segment higher up in the cord than the spinal nuclei of the flexors of the wrist and flexors of the fingers, which latter are also stated to be associated together in the cord. Thus Gowers[6] gives the segmental supply of those muscles as follows:—

$$\left.\begin{array}{l}\text{Triceps}\\ \text{Extensors of Wrist}\\ \text{Extensors of Fingers}\end{array}\right\} = \text{C. 6 and C. 7.}$$

$$\left.\begin{array}{l}\text{Flexors of Wrist}\\ \text{Flexors of Fingers}\end{array}\right\} = \text{C. 7 and C. 8.}$$

and Horsley[7] makes the following arrangement:—

$$\left.\begin{array}{l}\text{Triceps}\\ \text{Extensors of Wrist and Digits}\end{array}\right\} = \text{C. 7.}$$

$$\text{Flexors of Wrist and Digits} = \text{C. 8.}$$

Kocher,[8] on the other hand, distributes the same muscles as follows:—

$$\left.\begin{array}{l}\text{Triceps}\\ \text{Extensors of Wrist}\\ \text{Flexors of Wrist}\end{array}\right\} = \text{C. 7.}$$

$$\left.\begin{array}{l}\text{Extensors of Fingers}\\ \text{Flexors of Fingers}\end{array}\right\} = \text{C. 8.}$$

Thorburn[9] gives the following arrangement:—

Triceps = C. 6.
Extensors of Wrist = C. 7.
Flexors of Wrist = C. 8.

He does not locate the flexors and extensors of the fingers.

Our results are at variance with the statements of all those writers. In the above case the extensors and flexors of the wrist were unaffected from the outset, whilst the extensors and flexors of the fingers and thumbs were completely paralysed. It is, therefore, beyond doubt that the correct grouping of those muscles is one which places the *extensors and flexors of the wrist together* and *above the seventh cervical segment*, whilst the *extensors and flexors of the fingers and thumbs* are *at the seventh segment.*

Kocher, it is true, places the extensors and flexors of the wrist together at a level one segment higher than the extensors and flexors of the fingers, but he localises the former at the seventh and the latter at the eighth segment, whereas our case shows that such an arrangement is one segment too low, and that the extensors and flexors of the wrist really belong to the sixth cervical segment.

Nextly as to the triceps muscle. Both Horsley and Kocher place that muscle in the seventh cervical segment only, whilst Thorburn places it in the sixth only. Our case, however, shows that since the muscle, after being at first totally paralysed, subsequently regained part of its motor power, it is probably represented both in the sixth and seventh segments.

With regard to the pectoralis major, it is well known that the clavicular and sternal heads are really two distinct muscles. In our case the sternal head was paralysed, whilst the clavicular was unaffected. The sternal head of the pectoral muscle would therefore seem to be innervated from the seventh cervical segment, whilst the clavicular head is supplied by the sixth and probably by the fifth also, as stated by Gowers.

The exact segmental level of the interossei cannot be determined from our case alone. So far as it goes, however, it tends to show that the spinal nucleus of the interossei is somewhat higher than that of the thenar and hypothenar muscles, since the faradic reactions of the interossei were diminished, whilst those of the thenar and hypothenar eminences were unaltered.

To sum up: our case seems to point to the following arrangement being probably the correct one, so far as these particular muscles are concerned :—

Muscles.	*Segments.*
Pectoralis Major :—Clavicular Head	C. 5 and C. 6.
Latissimus Dorsi	C. 6.
Extensors of Wrist	
Flexors of Wrist	
Triceps	C. 6 and C. 7 (chiefly C. 7).
Extensors of Fingers	C. 7.
Flexors of Fingers	
Extensors of Thumb	
Flexors of Thumb	
Pectoralis Major :—Sternal Head	
Interossei	Below C. 7.
Thenar and Hypothenar Muscles	Below Interossei.

The limit of anæsthesia in this case is of interest, inasmuch as it showed considerable variations before settling down to its final boundary, shown in fig. 3. A curious point also was that the upper limit of the absolute anæsthesia, for the first twelve days at least (*vide* figs. 1 and 2), was much lower behind than in front. (After the twelfth day the anæsthesia could no longer be mapped out on the back of the trunk, owing to the extension apparatus applied.) The significance of this is not clear. Whether it might have been due to the non-severance of a certain number of fibres of the posterior columns is open to question. But the anæsthesia was tested with care, and there can be no doubt as to the fact.

It will also be observed, from a comparison of the charts at different dates, that the upper limit of the slight anæsthesia at first corresponded to the seventh segment, whilst the absolute anæsthesia was considerably below that. Eleven days later, the upper border of the slight anæsthesia reached up to the sixth segment, whilst the absolute anæsthesia had mounted to the seventh. The subsidence of the anæsthesia, which occurred later, to the seventh segment, indicates that the temporary increase of anæsthesia above that level was probably due to some vascular or inflammatory change in the sixth segment, which afterwards passed away.

The permanent anæsthesia (*vide* fig. 3) includes within its limit the two ulnar fingers of each hand. It is important to note that in those fingers alone was there loss of the sense of position on passive movement. This would indicate that in a segmental anæsthesia of the fingers the loss of joint-sense corresponds accurately in distribution with the distribution of the cutaneous anæsthesia. This segmental arrangement of joint-anæsthesia has apparently not been pointed out by previous observers.

The patient's temperature throughout was normal, except during the occasional occurrence of bronchitis, when it became elevated to 103° or 104° F. For five days before death it was persistently subnormal, between 96° and 97° F.

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(2) Gowers. "Diseases of the Nervous System," vol. i., 3rd edition (Gowers and Taylor), pp. 264 and 271.
(3) Babinski. *Semaine Medicale*, Juillet 28, 1898.
(4) van Gehuchten. *Journal de Neurologie Belge*, Avril 5, 1898.
(5) Collier. Brain, 1899, vol. xxii., p. 71.
(6) Gowers. *Op. cit.*, pp. 40-41.
(7) Horsley. "Allbutt's System of Medicine," vol. vi., p. 859.
(8) Kocher. *Verletzungen der Wirbelsäule und des Rückenmarks. Mitth. aus den Grenzgebieten*, 1897.
(9) Thorburn. "Contribution to the Surgery of the Spinal Cord, 1889," p. 4.

PROCEEDINGS OF THE NEUROLOGICAL SOCIETY OF LONDON.

At a Clinical Meeting held at 11, Chandos Street, W., on Thursday, March 15, 1900, at 8.30 p.m., the following cases were shown :—

Dr. F. E. Batten.—*Case of congenital cerebellar defect.*

D. S., aged 4 years, was brought to the hospital because she could not walk. She was the first and only child, and instruments had been used at her birth. The mother had had no miscarriages, and had been in good health while carrying the child. The child has never had any illness; she did not begin to use her hands till she was 12 months old.

When first seen, early in 1899, she was a well-nourished child with rather a large head. She was unable to walk but could support her weight, and always tended to fall backwards; afterwards, when taught to put her legs forward, she exhibited a markedly incoordinate gait. The knee-jerks were active, there was no rigidity of the legs, there was no ankle-clonus, and the plantar reflex gave a fairly regular extensor response of the great toe. The movements of the arms were also markedly incoordinate. The intelligence was good and the child could speak in a babyish way. She had a good deal of difficulty in swallowing, and, in consequence, had to be fed very slowly. There was no nystagmus and the fundus was normal. The child was again seen in February, 1900, and was practically in the same condition except that the plantar reflex did not now give such a definite extensor response as when the child was first seen. The child's back was quite normal.

Dr. Farquhar Buzzard.—*A case of cerebral diplegia* (under the care of Dr. T. Buzzard at the National Hospital).

A female child, aged 14 months. Parents alive and healthy. The mother has had seven pregnancies, four of which have resulted in miscarriages at or before the fourth month. There are two healthy children and the patient is the result of the sixth pregnancy. No history of nervous disease in family.

Whilst pregnant of this child the mother was quite healthy except for an affection of the throat causing loss of voice during two months. Labour was easy but not precipitate. Child healthy at birth; no acute illness subsequently. A slight deformity of foot was noticed at one month; since then a gradually progressive inability to move all four extremities, with slight difficulty in swallowing and impairment of vision. Marked wasting recently.

Present condition.—Weight, 8 lbs. Microcephalic and undersized. Marked optic atrophy with no definite pathological changes in the retina. Retraction of head and opisthotonos; generalised rigidity with extension of legs and flexion of arms. Feet dorsi-flexed and everted. Fingers flexed.

Dr. Risien Russell.—(1) *Case of functional wryneck, with clonic spasm of the palate.*

Female, aged 30 years, married. Is seven months pregnant. Has previously borne healthy children. Came under observation about seven weeks ago complaining of a clicking noise which had existed in her head since last May. Her head has also been twisted to the right, and drawn backwards; sometimes it has been twisted to the left. Her condition has made her very miserable, the clicking noise has prevented her from sleeping properly, and she has been losing flesh. No family history of nervous disease. No shock or worry preceded development of present condition, which consists in rapid clonic spasm of the palate, which is responsible for the clicking sound complained of, and which can be heard at some distance from the patient; and torticollis, the chin being usually turned to the right, and the head drawn backwards.

(2) *Two cases of Thomsen's disease* (*myotonia congenita*) in a Hebrew brother and sister. No history of similar affection of other members of the family. No known history of nervous affections. The labours were natural; the children were not backward in walking and talking, and they have neither of them been subject to fits.

(*a*) Male, aged 15½ years. Poorly developed for his age. Natural until 5 years old, when present difficulty in performing movements was first noticed. Condition gradually became more pronounced. Always most marked on first getting up in the morning, when movements of arms, as well as those of legs, are hampered by stiffness of the muscles. As successive movements are performed the stiffness becomes less and less marked. During the day the difficulty is chiefly noticed in the inferior extremities, progression being hampered by the stiffness which always comes on when movements are first attempted after a period of rest, and which are the more pronounced the longer the preceding period of inactivity. In him, as in his sister, the difficulty is best seen on attempting to mount a flight of stairs, the feat becoming more and more easy as they near the top. On closing the eyes tightly he has difficulty in opening them again, and after he flexes his fingers he can only relax the grasp slowly, in that the persisting contraction of the flexors prevents the full effect of the action of the extensors from being immediately realised. On withdrawing the tongue into the mouth after it has been protruded he experiences a stiff feeling in the organ. There is no permanent spasticity, and the tendon-jerks are natural. Tested by moderate currents the muscles show no notable alteration of the electrical reactions except that with galvanism A.C.C. is as readily obtained as K.C.C.

(*b*) Female, aged 5½ years. Natural development. Phenomena similar, but less marked than in her brother. The condition was first noticed about the age of 4 years, and now, sixteen months since that time, is more pronounced than when she first came under observation about four months ago. The resulting stiffness is less marked than in her brother, and a longer preceding period of inactivity is required to allow of its becoming manifest on attempts at movement.

Dr. EDWIN BRAMWELL.—*Two cases of myasthenia gravis* (under the care of Dr. T. Buzzard at the National Hospital).

(I.) Male, aged 40, schoolmaster. Illness began seven years ago with weakness in fingers of right hand; later, nasal voice, ptosis, difficulty in swallowing. Five years ago legs and arms weak, diplopia, difficulty in coughing and mastication, attacks of dyspnœa and palpitation. Fatigue, cold, and mental excitement all increase intensity of symptoms.

State.—Intelligent man, indistinct nasal speech, upper and lower facial weakness on both sides, diplopia, right-sided ptosis, defective upward movement of eyes, external recti weak, pupils react perfectly, jaws easily tired, tongue moves freely, palate movements and reflex action poor. Weakness of neck, arm and leg muscles, no muscular atrophy or fibrillary tremor. Myasthenic reaction present, arm-jerks poor, knee-jerks active, not exhausted by tapping. Sensation, sphincters, urine and other organs healthy.

(II.) Female, aged 24, housemaid. Anæmic for eighteen months. First symptom, weakness in legs one year ago; soon after developed weakness in arms, nasal speech, ptosis, diplopia, difficulty in mastication, coughing and swallowing.

State.—Double ptosis, ocular movements good, nystagmoid movements on lateral deviation, orbiculares palpebrarum very weak, tongue and palate move well but are soon exhausted, extremities weak, no atrophy, myasthenic reaction present, deep reflexes active, sensation and sphincters unaffected.

Dr. JAMES COLLIER.—*A case of muscular atrophy in the upper extremities* (under the care of Dr. Hughlings Jackson at the National Hospital).

A woman, aged 23 years. A very marked family history of tuberculous disease. Weakness and wasting commencing in the hands and spreading to the fore-arms of fifteen months' duration; severe pain in hands running along ulnar borders of both upper extremities of six months' duration; dull pain in lower cervical spine.

Spinal column natural. Great weakness and wasting in the thenar and hypothenar muscles, and complete paralysis of extensors of fingers. Extensors of wrist and the long extensor of the thumb escape. Slight anæsthesia over the eighth cervical and first dorsal root areas. The muscular is slowly progressive. The patient presents no other physical signs.

AT the Pathological Meeting held at 11, Chandos Street, on Thursday, May 10, 1900, the following specimens were shown:—

Dr. WAKELIN BARRATT.—Sub-dural cyst compressing the right hemisphere.

Dr. F. E. BATTEN.—Series of mounted specimens of some of the grosser pathological changes met with in the nervous system.

Dr. ALEXANDER BRUCE.—Tumour of the third ventricle associated with paralysis of conjugate movements of the eyes upwards and downwards, lateral movements being preserved.

Dr. JAMES TAYLOR.—Changes in the nerve-cells of the third and sixth cranial nerves from a case of ophthalmoplegia externa in which there were difficulties in articulation and swallowing.

Dr. J. S. COLLIER.—(1) Bone from a case of leontiasis ossea and photographs of the patient.

(2) The skull from a case of syringo-myelia simulating leontiasis ossea.

(3) Endothelioma of skull.

BRAIN.

PART II., 1900.

Original Articles and Clinical Cases.

HYPNOTIC AND POST-HYPNOTIC APPRECIATION OF TIME; SECONDARY AND MULTIPLEX PERSONALITIES.

BY J. MILNE BRAMWELL, M.B., C.M.

I COMMENCED to employ hypnotism as a therapeutic agent in 1889, and in less than two years treated over 500 patients; of these 48 per cent. became somnambules, *i.e.*, were unable when hypnosis terminated to recall the events of hypnotic life. Having observed that the curative effect of suggestion was increased by prolonged hypnosis, I frequently suggested to my patients that they were to remain in that state until a given hour—usually that of their next meal—and then left them. Although rarely present at the conclusion of the experiment, I obtained ample and trustworthy evidence that hypnosis invariably terminated at, or within a few minutes of, the hour indicated, and thus accidentally discovered that deep hypnosis was associated with an increased appreciation of time. These observations—the by-product of therapeutic work—led to more careful experiment with somnambules, the majority of whom were males and all in good health. The following were the usual suggestions given: (1) A simple act was suggested during hypnosis which was to be carried out at a given time before that state terminated. (2) The subject was told during hypnosis that this state was to terminate at a specified future hour. (3) The performance of a simple act at a given hour after the termination of hypnosis was suggested. (4) Awakening from natural sleep at a given hour was suggested during hypnosis. (5) The subject was told in the waking state that he was to pass into the hypnotic condition at a given hour, remain hypnotised for a specified length of time and perform certain simple acts at stated intervals; then pass again into the normal state and remain in it for a specified time, and again pass into the hypnotic condition. These experiments, continued from 1889 to the present date, have been frequently repeated before competent observers. The majority of the suggestions were executed at the moment indicated, while in the remainder the error in time appreciation rarely exceeded five minutes. In every instance, except those referred to in group No. 4, the subjects were carefully watched from the beginning to the end of the experiment.

Similar phenomena have been observed by nearly all who have done practical hypnotic work, and I have seen experiments resembling those just cited reproduced in various foreign cliniques. Two, formerly regarded as the most remarkable of their kind, were made by Beaunis and Liégeois. In one of these a visual hallucination appeared after a suggested interval of 172 days, and in the other after 365. The late Professor Delbœuf, however, pointed out in reference to all such experiments that even in the longest a fixed date had been impressed upon the subject's mind. Thus, Beaunis' subject was told that the 172nd day was New Year's Day, and Liégeois' was impressed by the fact that the suggestion was to be executed in a year from the time it was given. The experiments, therefore, did not involve the carrying out of a suggestion after the lapse of so many days, which the subjects were supposed to count as they passed, but simply on the arrival of a fixed and easily recognised date. This objection applies with great force to my earlier cases. In every instance a specified hour was suggested; and, in order that the subjects might be conveniently watched, the time involved rarely exceeded a few hours. This point will be again referred to in treating of the theoretical explanation of the appreciation of time. Meanwhile, I wish to draw attention to the experiments made by Delbœuf with the object of eliminating an easily recognised fixed date from the suggestions.

DELBŒUF'S EXPERIMENTS.

These occupied a week, from Saturday, October 2, to Saturday, October 9, 1886. His subjects were his two maid-servants, J. and M., sisters, aged respectively 20 and 23. All the experiments were of a similar character; from time to time during hypnosis the subjects were told that they were to do something at the expiration of a certain number of minutes, an interval of waking life always intervening between the suggestion and its fulfilment:—

Exp.[*] 1.—Sat., Oct. 2, 1886; subject J.; time 6 a.m. *Sug.:* At the expiration of 350 m. J. was to ask Delbœuf if she should harness the donkey. Delbœuf's wife was ill and went out in an invalid carriage drawn by a donkey, but J. had nothing to do with it; thus her question would be unusual. *Res.:* The impulse to ask the question came into J.'s mind at the time it was due, but she successfully resisted it.

Exp. 2.—Subject M.; time 8 a.m. *Sug.:* At the expiration of 350 m. M. was to ask Madame Delbœuf if she would like to go out. Under the circumstances the question would be an unusual one. *Res.:* At 1.50, the hour indicated, M. was impelled to ask the question, but as she happened to be in the village on an errand, was unable to do so. She returned at 2.30 and carried out the suggestion.

Exp. 3.—Mon.; subject J.; time 9.15 a.m. *Sug.:* In 900 m., *i.e.*, at 12.15 a.m., J. was to go into the bedroom of one of Delbœuf's children and pull his ear. *Res.:* Suggestion carried out 95 m. too soon.

Exp. 4.—Subject M.; time 9.25 a.m. *Sug.:* M. was to embrace Mlle. H. Delbœuf at the expiration of 700 m. *Res.:* Twenty-five m. before the suggestion fell due M. looked for Mlle. H. Delbœuf in order to embrace her, but could not find her.

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[*] Exp. = Experiment. Sug. = Suggestion. Res. = Result. d. = days. h. = hours. m. = minutes.

Exp. 5.—Subject M.; time 10.4 p.m. *Sug.:* In 900 m. M. was to embrace Mlle. C. Delbœuf. *Res.:* At the time indicated, *i.e.*, 1.4 on Tuesday afternoon, M. was having her lunch with the other servants when she suddenly got up from the table, sought and found Mlle. C. Delbœuf and carried out the suggestion.

Exp. 6.—Tues.; subject J.; time 6.30 a.m. *Sug.:* At the expiration of 1,600 m. J. was to pull the cook's nose. *Res.:* Suggestion carried out 60 m. too soon.

Exp. 7.—Subject M.; time 6.45 a.m. *Sug.:* At the expiration of 1,150 m. (Wed., 1.55 a.m.) she was to go into the cook's bedroom and pull her by the ear. (The cook was told what was likely to happen.) *Res.:* At the exact hour the subject had a strong impulse to carry out the experiment, but resisted this until 4.15 a.m., when she gave in and went to the cook's room. The cook laughed, whereupon M. said: "If you laugh I shall pull your ear."

Exp. 8.—Wed.; subject J.; time 9.55 a.m. *Sug.:* At the expiration of 1,300 m. (Th., 7.35 a.m.) J. was to ask Madame Delbœuf if she would like to have her hair dressed. *Res.:* Suggestion carried out 69 m. too soon.

Exp. 9.—Subject M.; time 6.55 a.m. *Sug.:* At the expiration of 1,500 m. (Th., 7.55 a.m.) M. was to ask Madame Delbœuf if she required anything. *Res.:* Suggestion carried out with absolute accuracy.

Exp. 10.—Friday; subject M.; time 6.30 a.m. *Sug.:* M. was to feel sleepy at 10 p.m.; go to bed and sleep profoundly. *Res.:* Correct.

Exp. 11.—Subject J.; time 9.15 a.m. *Sug.:* At 11 p.m. J. was to go into M.'s room and give her a complicated suggestion to be carried out at 5.30 next morning. *Res.:* J. went to bed at 10 p.m. in her own room and quickly fell asleep. At 10.50 p.m. (10 minutes too early) she went to her sister as suggested, but could not afterwards recall what she had said or done.

Exp. 12.—Subject M. *Sug.:* M. was to execute the orders just referred to at 5.30 a.m. She did nothing, however, beyond carrying out the first part of the suggestion, *i.e.*, that she should go to bed and sleep profoundly, and was unable to remember whether her sister had said anything to her or not.

Exp. 13.—Sat.; subject J.; time 9.30 a.m. *Sug.:* At the expiration of 3,300 m. J. was to ask Delbœuf if she should carry a small ladder to the pear tree. *Res.:* The impulse to ask the question arose 90 m. too late, but J. did not give way to it.

Exp. 14.—Subject M.; time 10 a.m. *Sug.:* Similar to the last to be executed after a like interval. *Res.:* Identical with the above, but 90 minutes too soon.

Summary.

There were in all fourteen experiments. The suggestions, to be carried out after the lapse of 350, 900, 1,600, 1,150, 1,300 and 3,300 minutes respectively, were made at varying hours of the day and night, while some fell due at night after the lapse of several days.

Results.

Three of the suggestions were fulfilled at the moment they fell due; four were carried out, but not at the exact time. In three an impulse to carry out the suggestion arose at the right moment. In one of these, the subject successfully resisted the suggestion, in another, she was accidentally prevented from executing it, while in the third, she struggled against it for two hours and twenty minutes and then carried it out. In three, the impulse to carry out the suggestion arose, but not at the correct time. In one of these cases accidental circumstances alone prevented the suggestion from being carried out, but in the two others, the subject successfully resisted it. One alone, No. 12, failed completely, but this may have been due to the fact that No. 11 was not fulfilled in its entirety, *i.e.*, it is doubtful whether J. gave the requisite orders to M. As, however, the essential fact in the experiments was not the actual carrying out of trivial and sometimes absurd suggestions, but the patient's recognition of the terminal time, the cases in which an impulse arose at the correct moment must be classed amongst the successes. The number of these is thus raised to six, while of the eight remaining experiments seven were partially successful. Of the latter four were carried out and an impulse to execute the suggestion arose in the other three, but in none was the time accurate; the error varied from a tenth to a thirty-seventh of the interval.

Remarks.

J. and M. were strong healthy peasant girls, who had frequently been hypnotised and were both good somnambules. At an earlier date, Delbœuf had made the following experiment with J. After explaining what he proposed to do, and obtaining her consent in the waking state, he hypnotised her, extended her arms on a table, and suggested that the right should be insensible to pain. Each arm was then burnt with a red-hot bar of iron, 8 millimetres in diameter, the extent and duration of its application being identical in both, but there was pain in the left arm alone. The burns were bandaged and J. sent to bed. During the night the pain in the left arm continued, and next morning there was a wound on it, 3 centimetres in diameter, with an outer circle of inflamed blisters. On the right there was only a defined eschar, the exact size of the iron and without inflammation or redness. The day following the left arm was still more painful and inflamed; analgesia was then successfully suggested, when the wound soon dried and the inflammation disappeared.

Later J. married and was 29 years of age when her first child was born. She was attended by Dr. Fraipont, Lecturer of Gynæcology at the University of Liège, while Delbœuf induced hypnosis and made suggestions of analgesia. When J. was aroused from the hypnotic state, after the birth of the child, she was unable to recall anything that had occurred.

J. and M. were very imperfectly educated and could with difficulty tell the time by the clock. It was impossible for them to at once reduce such a large number of minutes as 400 into hours and they were obliged to proceed by successive additions, thus:—1 hour = 60 minutes; 1 hour and 1 hour makes 60 + 60 = 120; 120 + another hour makes 180, and so on. Before reaching 360 they had often made mistakes, and, no matter what method they adopted, were absolutely incapable of reducing such numbers as 1,600 and 1,150 minutes into hours. Further, supposing they recalled the suggestion on the termination of hypnosis and noted what o'clock it was—which they neither did nor could do—they would still, for example, have to determine by mental calculation the hour which corresponded to 6.45 p.m., increased by 1,150 minutes, a feat entirely beyond their powers.

Later, in order to discover whether J.'s hypnotic arithmetical powers exceeded her normal ones, Delbœuf put the following problems to her during hypnosis:—(1) "Turn 350 minutes into hours." Answer: "Six hours. No, five and a half hours." (2) "Turn 1,200 minutes into hours." A. "Fifteen hours. No, twelve and a half hours." (3) "Turn 150 minutes into hours." A. "Two and a half hours." (4) "Turn 240 minutes into hours." A. "Two hours." "Think!" Answer, after two minutes, "Four hours." (5) "Turn 300 minutes into hours." Answer, after five seconds' calculation, "Four and a half hours." Then, after a further calculation, "Five and a half hours." Finally, "Five and three quarter hours." Delbœuf asked J. to explain the last calculation to him. She replied: "This makes five and a half hours plus 3 times 10, which makes five and a half hours exactly." Delbœuf tried to help J. as follows:—"How much is 60 + 60?" Answer, "120 minutes." "120 + 60?" A. "180 minutes." "180 + 60?" Answer, after a long hesitation, "240 minutes." "240 + 60?" A. "290 minutes." J. had spent ten minutes over attempting to solve the last problem and showed great signs of fatigue. Delbœuf did not consider it necessary to push the questions further. It is to be noted that M. was a somewhat better arithmetician than J., and that, in the experiments referred to, her results were more accurate than J.'s.

FURTHER TIME EXPERIMENTS.

The following were inspired by Delbœuf's, and the results were so remarkable that I feel justified in giving as many details as possible, in order to present a fairly complete picture of the subject of the experiments, and of the circumstances under which they were carried out:—

Miss A., aged 19, was sent to me by Dr. de Watteville for hypnotic treatment, on Sept. 2, 1895. Her health had been good up to twelve months previously, when violent muscular tremor of the right arm and hand commenced. After a few weeks this spread to the right leg, and then to the left arm and leg; the tremor ceased during sleep, but only then, while walking was always difficult and painful. There was almost constant diffused headache. During the last four months, there had been frequent attacks of pain in the region of the heart. After the patient had looked at a bright object—especially anything blue—everything else appeared of that colour; this impression persisted for about an hour, while its disappearance was always sudden and accompanied by a feeling of faintness. Menstruation began at 11, and was always painful, and there had been obstinate constipation from infancy. Her illness began after over-exertion and mental strain, the result of nursing a relative who died. There had been no previous hysterical symptoms and the family history was good.

Treatment.—Electricity, massage, careful drugging and change of air.

Result.—No improvement.

I succeeded in inducing fairly deep hypnosis at the first attempt; and this was repeated on September 4, 5, and 6, when the tremor almost entirely disappeared. From then to October 30 she was hypnotised on seven occasions. *Res.:* No tremor or other morbid symptoms. Bowels regular. Last period free from pain. Fourteen pounds gained in weight since beginning of treatment. No abnormal colour perceptions. Returned to work.

Remarks.—Hypnosis became more profound each time it was induced, and at the seventh séance Miss A. reached the stage of somnambulism, *i.e.*, she was unable in the normal state to recall the events of hypnotic life. From this date she could at once be made analgesic or anæsthetic by suggestion; touching the cornea or tickling the back of the throat with a feather produced no reflex, and the passing of a needle deeply into the flesh was unattended by pain.

During treatment suggestions had been made fixing the hour at which Miss A. was to fall asleep at night and the moment at which she was to wake in the morning. As these were remarkably successful, it occurred to me that she might prove a good subject for experiments similar to those of Delbœuf. Miss A. was an intelligent girl who had received an ordinary School-board education, and her arithmetical powers were in keeping with this; she could do ordinary sums in multiplication and subtraction with the aid of a pencil and paper, but failed, unless they were extremely simple, to solve them mentally. Notwithstanding this, she asserted that she had been the best in her class at mental arithmetic. She possessed no particular aptitude for appreciating the passage of time.

Exp. 1.—Nov. 5, 1895; time 4 p.m. Suggestion given during hypnosis: At the expiration of 5 h. and 20 m. Miss A. was to make a cross on a piece of paper, and write down the time she believed it to be without looking at clock or watch.—*Res.:* The suggestion was carried out the minute it fell due. *Remarks:* On this occasion I did not say anything to Miss A. about the experiment, either before or after hypnosis, and, being a somnambule, she retained in her waking consciousness no recollection of the suggestion. I told her mother its nature, but not the time at which it should be fulfilled. At 9.15 the same evening her mother noticed that Miss A. was restless, and asked her what was the matter. She replied, "I feel I must do something, but cannot tell what." At 9.20 p.m. she rapidly made a cross with a pencil and wrote "20 minutes past 9" on a piece of paper, at the same time saying, "It's all silliness." There was no clock in the room, but her mother went into the next room where there was one, and found that the time was 9.20. When I again saw Miss A., I explained the nature of the experiments I proposed making, and instructed her to carry a pencil and paper during the day and to put them by her bedside at night. I did not describe the experiments as anything extraordinary, but simply told her that hypnotised subjects were often able to appreciate time, and that I wished to see whether she could do so. No pecuniary or other reward was promised or given. I told her I should make these suggestions from time to time, but not on each occasion she visited me. I neither told her in the waking condition that suggestions had been made, nor informed her relatives when I made them, nor what they were. They knew that suggestions of this nature were given frequently, but only became acquainted with them by seeing Miss A. carry them out, or by hearing from her that she had done so. Before making the suggestions, I wrote them down in my case book, and, when Miss A. again visited me, I copied into it what she had written on the different pieces of paper. In many instances I did not calculate when the suggestions fell due, and in others the calculations I made at the time were proved to be erroneous, the results of the experiments in these cases being only determined when the series was completed.

The experiments which followed were all of the same character, *i.e.*, during hypnosis Miss A. was told that, at the expiration of a certain number of minutes, she was to make a cross and write down the hour she believed it to be without consulting the clock, an interval of waking life always intervening between the suggestion and its fulfilment. The simple and uniform character of my experiments is due to the fact that Delbœuf's subjects resisted suggestions that were distasteful to them. The idea of making a cross on a piece of paper excited no opposition in Miss A.'s mind, while the fact that she recorded in writing the time at which the suggestion was fulfilled, especially when this was witnessed by others, put me in possession of evidence of a certain value. The arithmetical problems involved in the first one or two of the following experiments were comparatively simple. In No. 3, for example, as Miss A. could easily tell when 24 hours fell due, the suggestion practically resolved itself into one to be fulfilled in 100 minutes. Soon, however, the experiments became complicated and involved much more difficult problems in arithmetic.

Exp. 2.—Nov. 28, 1895; 2 p.m. *Sug.:* to be fulfilled in 320 m. *Res.:* Correct. *Remarks:* The suggestion was carried out at 7.20 p.m. when the patient was in a friend's house. She had no watch with her and the clock in the room was wrong.

Exp. 3.—Dec.4; 3.15 p.m. *Sug.:* in 24 h. and 100 m. *Res.:* Correct. *Remarks:* When in a friend's house the following afternoon she carried out the suggestion at 4.55. She then asked the time. Her friend looked at her watch and told her, whereupon she remarked, "Your watch is 3 minutes fast." This was the case.

Exp. 4.—Dec. 12; 3.20 p.m. *Sug.:* in 24 h. 1,440 m. *Res.:* 3.20 p.m. Sat., Dec. 14: Correct.

Exp. 5.—Wed., Dec. 18; 3.45 p.m. *Sug.:* in 24 h. 2,880 m. *Res.:* 3.45 p.m., Sat., Dec. 21: Correct.

Exp. 6.—Tues., Dec. 24; 2.55 p.m. *Sug.:* in 30 h. 50 m. *Res.:* 9.45 p.m., Wed., Dec. 25: Correct.

Exp. 7.—Tues., Dec. 24; 3.10 p.m. *Sug.:* in 7,200 m. *Res.:* 3.10 p.m. Sun., Dec. 29; Correct. *Remarks:* When No. 7 was fulfilled the patient was teaching a Sunday school class, when she suddenly felt an impulse to make a cross and mark the time. It was only after doing so that she looked at the clock, which was behind her.

Exp. 8.—Tues., Dec. 31; 3.45 p.m. *Sug.:* in 4,335 m. *Res.:* 4 p.m. Fri., Jan. 3, 1896: Correct.

Exp. 9.—Dec, 31, 1895; 4 p.m. *Sug.:* in 11,525 m. *Res.:* 11.5 a.m., Wed., Jan. 8: Wrong. *Remarks:* The result ought to have been 4.5 p.m., Jan. 8. I re-hypnotised Miss A. on that day and asked her to recall the suggestion I had made on Dec. 31. She said it was to be executed in 11,225 m.; it is possible that I had made a mistake, but not at all likely, as I read the suggestion to her with the figures before my eyes. The supposed suggestion of 11,225 m. had been carried out correctly.

I now attempted to find out during hypnosis the patient's mental condition in reference to these suggestions. In reply to my questions she informed me:—(1) That when the suggestions were made in hypnosis she did not calculate when they fell due; (2) That she did not calculate them at any time afterwards during hypnosis. (3) That she had no recollection of them when hypnosis terminated. (4) That no memory of them ever afterwards arose in the waking state. (5) That shortly before their fulfilment she always experienced a motor impulse, *i.e.*, her fingers moved as if to grasp a pencil and to perform the act of writing. (6) That this impulse was immediately followed by the idea of making a cross and writing certain figures. (7) That she never looked at clock or watch until after she had made her record.

Experiments, Wed., Jan. 8, 1896.—No. 10: 4.5 p.m. *Sug.:* in 4,417 m.—No. 11: 4.5 p.m. *Sug.:* in 11,470 m.—No. 12: 4.30 p.m. *Sug.:* in 10,070 m.

As Miss A. stated in hypnosis that she made no calculations, in order to vary the experiments I asked her, as soon as I made the suggestions and before terminating the hypnosis, to calculate when they would fall due and tell me the result. She replied as follows: No. 10, in 3 d. 37 m., or 23 m. to 5 next Saturday afternoon.—No. 11, in 187 h. 50 m., or 7 d. 9 h. 50 m. Next Wednesday morning at 5 m. to 12.—No. 12, in 1,067 h. 40 m., or 6 d. 23 h. and 40 m. 4.20 p m. next Wednesday.

Miss A.'s calculation in No. 10 was 1 h. 5 m. too early. The interval (which was 1 h. too short) having apparently been calculated from 4 o'clock, instead of 4.5 p.m. In No. 11 her calculation was 1 d. 3 h. 20 m. too early. Here (1) 11,270 was taken instead of 11,470, and hence the interval was calculated to be 187 h. 50 m.; equalling 7 d. 19 h. 50 m. (2) 7 d. 9 h. 50 m. was given instead of 7 d. 19 h. 50 m. The time falling due was then calculated with this interval (7.19.50), but (3) a mistake of 1 d. was made.

In No. 12 her result was correct, but did not correspond with her calculation. 10,070 m. equals 167 h. 50 m., not 1,067 h. 40 m. Here (1) a cypher was wrongly inserted and (2) 40 m. miscalculated for 50. The latter error was repeated when 6 d. 23 h. 40 m. was given instead of 6 d. 23 h. 50 m.—*Res.:* No. 10, Sat., Jan. 11, 5.42 p.m.: Correct.—No. 11, Thur., Jan. 16, 3.15 p.m.: Correct.—No. 12, Wed., Jan. 15, 4.20 p.m.: Correct.

Remarks.

As the subject had wrongly calculated during hypnosis the time the suggestions fell due, I concluded that she had thus fixed these dates in her own mind and would carry out the experiments in accordance with them. My astonishment was great when they were executed correctly. I re-hypnotised Miss A. and said to her, "You did not carry out these suggestions at the hours you told me they would fall due. Why was this?" She replied, "What I told you was all wrong." "How do you know the other results are right?" "I can't tell you, I only feel that they are." Further questioning elicited no memory of the processes by which the original mistakes had been corrected. Miss A. assured me that she had never thought of the suggestions from the time they were made; she simply fulfilled them in response to an impulse to write down the figures, and while doing so, neither recalled her calculations nor even the suggestions themselves.

When No. 12 was fulfilled, Miss A. had been hypnotised in my room for an hour and had had no opportunity of consulting the clock. Exactly at 4.20, without waking or opening her eyes, she said she had to make a cross and put down the time—this was preceded by the movement of the fingers already described. From this date I arranged that some of the experiments should fall due when Miss A. visited me, but not, it is important to note, every time she came. They were fulfilled either in the normal waking state or in hypnosis, and Miss A. recorded them herself in my case book. I then at once compared her figures with the actual time and entered the result, this being nearly always witnessed and signed by others. From this date several suggestions were made at each séance. In some cases, the same hour was given as the starting point of all the experiments; in others, varying and even imaginary ones were chosen. In the latter case, the subject was told the actual time, but ordered to carry out the experiment from, say, 2.15 p.m. of the previous day.

Experiments, Wed., Jan. 15, 4.45 p.m.—No. 13, from 4.45 p.m. *Sug.:* in 4,453 m.—No. 14, from 2 p.m. *Sug.:* in 10,470 m.—No. 15, from 2 p.m. *Sug.:* in 10,060 m.

At the time the suggestions were made the patient was again asked in hypnosis to calculate when they would fall due and replied rapidly:—"No. 13, in 722 h. and 33 m., or 11.15 p.m. next Wednesday." "No. 14, in 197 h. and 30 m., or 4.5 p.m. next Wednesday." "No. 15, in 8 d., 5 h. and 30 m., or 4.25 p.m. next Wednesday."

In No. 13, Miss A.'s calculation was 4 d. 4 h. 17 m. too late. 4,453 m. equals 74 h. 13 m., not 722 h. 33 m. Perhaps 4,453 was mistaken for 43,353 equalling 722 h., 33 m. The time of falling due had been calculated from the interval of No. 14.

In No. 14, her calculation was 4 h. 25 m. too early. 10,470 m. equals 174 h. 30 m., not 197 h. 30 m. The time of falling due was also wrong. There is no explanation for either of these independent errors.

In No. 15, her calculation was 1 h. 45 m. too late. The wrongly calculated interval, 8 d. 5 h. 30 m., corresponded to the wrongly calculated 197 h. 30 m. of No. 14; this interval had apparently remained in the mind. The time of falling due had been calculated with 4.45 as initial time, as in No. 13, instead of 3.0.

Results.—No. 13, Sat., Jan. 18, 6.58 p.m. Correct.—No. 14, Wed., Jan. 22, 8.30 p.m. Correct.—No. 15, Wed., Jan. 22, 2.40 p.m. Correct.

Remarks.—Again the subject's miscalculation did not affect the accuracy of her results, and questioning in hypnosis again failed to revive any memory of the processes by which these had been reached.

Experiments, Wed., Jan. 22, 4.5 p.m.—No. 16. *Sug.:* in 20,180 m.—No. 17. *Sug.:* in 20,160 m.—No. 18. *Sug.:* in 20,140 m. Miss A.'s calculations in hypnosis. "No. 16, in 336 h. 20 m., or 13 d. 20 m. Tues., Feb. 4, at 4.25 p.m." "No. 17, Tues., Feb. 4, at 4.5 p.m." "No. 18, Tues., Feb. 4, at 3.45 p.m." In each instance these calculations were 1 d. too early, but in No. 16, 20, 180 m. was correctly given as 336 h. 20 m.

Results.—No. 16, Feb. 5, 4.25 p.m. Correct.—No. 17, Feb. 5, 4.5 p.m. Correct.—No. 18, Feb. 5, 3.45 p.m. Correct.

Remarks.—On Wed., Feb. 5, I hypnotised Miss A. at 3 p.m. At 3.45, without passing from the hypnotic state, she made a cross and wrote down the correct time. I aroused her at 4 o'clock and she carried out the remaining experiments correctly at 4.5 and at 4.25.

Experiments, Wed., Feb. 5, 4 p.m.—No. 19. *Sug.:* in 10,050 m.—No. 20. *Sug.:* in 10,080 m.—No. 21. *Sug.:* in 10,090 m.—No. 22. *Sug.:* in 840 m.—No. 23. *Sug.:* in 900 m.

Miss A.'s calculations in hypnosis: "No. 19, Wed., Feb. 12, 3.30 p.m." "No. 20, Wed., Feb. 12, 4 p.m." "No. 21, Wed., Feb. 12, 4.10 p.m." "No. 22, Thur., Feb. 6, 6 a.m." "No. 23, Thur., Feb. 6, 7 a.m."

The above, made almost immediately, were correct in every instance.

Results.—No. 19, Wed., Feb. 12, 3.30 p.m. Correct.—No. 20, Wed., Feb. 12, 4 p.m. Correct.—No. 21, Wed., Feb. 12, 4.10 p.m. Correct.—No. 22, Thur., Feb. 6, 6 a.m. Correct.—No. 23 Thur., Feb. 6, 7 a.m. Correct.

Remarks.—When Miss A.'s mother went to her bedroom on the morning of the 6th, she found her asleep and two pieces of paper on a table by the bedside. On each was a rough cross; on one the figure 6, on the other 7, both very badly written. Miss A. said she had not awakened during the night.

The other suggestions were carried out during hypnosis in my room, the time being marked by Miss A. in my note book and witnessed by others.

The five suggestions were given rapidly one after the other. These, and similar complicated ones, were never read to the subject more than twice, and sometimes only once.

I re-hypnotised Miss A. and questioned her about the suggestions which had been carried out during the night, presumably in natural sleep. She told me she remembered nothing about them, and afterwards, when suggestions were again carried out in natural sleep, her memory was equally at fault.

Experiments, Wed., Feb. 12.—No. 24, 3.30 p.m. *Sug.:* in 2,220 m.—No. 25, 3.30 p.m. *Sug.:* in 2,285 m.—No. 26, 3 p.m. *Sug.:* in 10,115 m.—No. 27, 3 p.m. *Sug.:* in 10,150 m.—No. 28, 4 p.m. *Sug.:* in 20,190 m.

Miss A.'s calculations in hypnosis: "No. 24, in 18 h. and 40 m., or 10.10 to-morrow morning.—No. 25, to-morrow morning at 11.15.—No. 26, next Wednesday at 25 m. to 4 p.m.—No. 27, next Wednesday at 5.30 p.m.—No. 28, a fortnight and half an hour."

The answers to Nos. 26, 27, 28, were given immediately. In No. 24, Miss A.'s calculation was 18 h. and 20 m. too early, but would have been correct if the interval suggested had been 1,120, instead of 2,220 m. In No. 25, her calculation was 18 h. 20 m. too early, but would have been correct had the suggested interval been 1,185, instead of 2,285 m. In No. 26, her calculation was correct. In No. 27, her calculation was 1 h. 20 m. too late. Here the interval seems to have been taken as 7 d. 150 m., instead of 10,150 m. In No. 28, her calculation was correct as far as it went, but the exact time of fulfilment was not given.

At the time I made the suggestions I also calculated when they would fall due, thus: No. 24, Feb. 14, 5 a.m. Wrong; half an hour too late.—No. 25, Feb. 14, 6.5 a.m. Wrong; half an hour too late.—No. 26, Feb. 19, 3.35 p.m. Right.—No. 27, Feb. 19, 4.10 p.m.: Right.—No. 28, Feb. 26, 4.25 p.m. Wrong; 5 m. too soon.

Res.: No. 24, Fri., Feb. 14, 4.30 a.m. Correct.—No. 25, Fri., Feb. 14, 5.35 a.m. Correct.—No. 26, Wed., Feb. 19, 3.35 p.m. Correct.—No. 27, Wed., Feb. 19, 4.10 p.m. Correct. No. 28, Wed., Feb. 26, 4.30 p.m. Correct.

Nos. 24 and 25 were fulfilled during sleep. On the 14th Miss A., on awaking, found papers by her bedside with 4.30 and 5.35 written on them. On the 19th she was hypnotised in my room at 3 p.m., and carried out Nos. 26 and 27 while in hypnosis. On both occasions she wrote the time in my note book, and this was witnessed. I asked her during hypnosis if she remembered my last suggestion (No. 28), made the previous week. She said she did and repeated it correctly, but stated she had never thought of it since, and did not know when it would fall due, or the number of minutes that had elapsed since it was given. She had apparently forgotten that, when the suggestion was given, she had calculated when it would fall due. No. 28 was executed correctly during hypnosis on February 26.

Experiments, Wed., Feb. 19.—No. 29, 3.30 p.m. *Sug.:* in 720 m.—No. 30, 3.30 p.m. *Sug.:* in 780 m.—No. 31, 3.30 p.m. *Sug.:* in 2,160 m.—No. 32, 3 p.m. *Sug.:* in 10,135 m.—No. 33, 3 p.m. *Sug.:* in 20,210 m.

Miss A.'s calculations in hypnosis: These, with the exception of No. 32, were all correct, and her replies were almost instantaneous. No. 32 was said to be due at 2.5 p.m. on Wed., Feb. 26. This was 1 h. 50 m. too early, and represented an interval of 7 d. less 55 m., instead of 7 d. plus 55 m.

Res.—No. 29, Thur., Feb. 20, 3.30 a.m. Correct.—No. 30, Thur., Feb. 20, 4.30 a.m. Correct.—No. 31, Fri., Feb. 21, 3.30 a.m. Correct.—No. 32, Wed., Feb. 26, 3.55 p.m. Correct.—No. 33, Wed., Mar. 4, 3.50 p.m., was written down at 3.48. The calculation, therefore, was correct, but the time appreciation 2 m. too early.

Remarks.—On awaking at 7 o'clock on the morning of the 20th, Miss A. found a piece of paper with 3.30 marked on it, and another with 4.30. On the morning of the 21st she found a piece of paper with 3.30 marked on it. She had no recollection of waking during the night, and, as usual, questioning in hypnosis failed to revive any memory of what she had done. The other suggestions were fulfilled in my room and witnessed by others.

Experiments, Wed., Feb. 26, 3.30 p.m.—No. 34. *Sug.:* in 2,140 m.—No. 35. *Sug.:* in 3,590 m.—No. 36. *Sug.:* in 5,030 m.—No. 37. *Sug.:* in 10,125 m.—No. 38. *Sug.:* in 10,100 m. —No. 39. *Sug.:* in 20,180 m.

Res.: No. 34, Fri., Feb. 28, 3.10 a.m. Correct.—No. 35, Sat., Feb. 29, 3.20 a.m. Correct.—No. 36, Sun., Mar. 1, 3.20 a.m. Correct.—No. 27, due Wed., Mar. 4, at 4.15 p.m., was not recorded.—No. 38, Wed., Mar. 4, 3.50 p.m., was written down at 3.48. Calculation therefore correct, but time appreciation 2 m. too early.—No. 39, Wed., Mar. 11, 3.50 p.m., was written down at 3.51½. Calculation therefore correct, but time appreciation 1½ m. too late.

Remarks.—These suggestions were only read to Miss A. once; she was then asked to repeat them, and did so correctly, with the exception of No. 37. She was told not to make any calculations. Nos. 34, 35 and 36 were executed during sleep, and the papers, as usual, were found at Miss A.'s bedside in the morning. It is to be noted that 3.50, March 4, the terminal time of No. 38, was also the time at which another suggestion, made a fortnight before, fell due, and which has already been recorded in its proper place. Miss A. stated at 3.48 that she had to make two crosses and to put down 3.50 twice. No. 37, due at 4.15 p.m., Wednesday, March 4, I have no record of. I am not certain whether this was my fault or Miss A.'s; I was hypnotising another patient when the suggestions were fulfilled, and I might well have omitted to enter that one; on the other hand, Miss A. might have failed to carry it out. Three suggestions fell due very quickly, and one of them, as we have seen, belonged to another series. When suggestions were made to fall due in a fortnight and I saw the patient in the week between, I sometimes questioned her in hypnosis as to the unfulfilled ones; she always assured me that she had never thought of them, did not know how much of the time had elapsed, nor when they fell due.

Experiments, Wed., Mar. 4, 3.45 p.m.—No. 40. *Sug.:* in 10,080 m.—No. 41. *Sug.:* in 10,055 m.—No. 42. *Sug.:* in 10,040 m.—No. 43. *Sug.:* in 750 m.—No. 44. *Sug.:* in 2,160 m.—No. 45. *Sug.:* in 2,195 m.—*Res.:* No. 40, Wed., Mar. 11, 3.45 p.m., was written down at 3.44. Calculation correct; time appreciation 1 m. too soon.—No. 41, Wed., Mar. 11, 3.20 p.m., was written down at 3.22. Calculation correct; time appreciation 2 m. too slow.—No. 42, Wed., Mar. 11, 3.5 p.m. Correct.—No. 43, Thur., Mar. 5, 4.15 a.m., during sleep. Correct.—No. 44, Fri., Mar. 6, 3.45 a.m., during sleep. Correct.—No. 45, Fri., Mar. 6, 4.20 a.m., during sleep. Correct.

Remarks.—When these suggestions were given Miss A. was not asked to calculate when they would fall due. Mr. Barkworth and Dr. Barclay were present when Nos. 40, 41 and 42 were fulfilled.

At this séance, March 11, fresh suggestions were made under the following conditions. Mr. Barkworth and Dr. Barclay were both put *en rapport* with Miss A., and it was agreed that they should each make two time suggestions, arranged so as to fall due at the next séance, when they promised to be present. These were given when I was out of the room, and I was not told what they were until after their fulfilment. The suggestions were as follows :—

Experiments, Wed., Mar. 11, 4 p.m.—No. 46. *Sug.:* in 21,400 m.—No. 47. *Sug.:* in 21,420 m.—No. 48. *Sug.:* in 21,428 m.—No. 29. *Sug.:* in 21,434 m.—*Res.:* No. 46, Thurs., Mar. 26, 12.40 p.m., was written down at 12.38. Calculation correct, time appreciation 2 m. too early.—No. 47, Thur., Mar. 26, 1 p.m., was written down at 12.59. Calculation correct, time appreciation 1 m. too early.—No. 48, Thur., Mar. 26, 1.8 p.m. Correct.—No. 49, Thur. Mar., 26, 1.14 p.m. Correct.

Remarks.—Miss A. was hypnotised at 12.30 p.m. on Thursday, March 26, and carried out the suggestions while in that condition. Mr. Barkworth and Dr. Barclay were both present and checked the time records. None of us, however, had any idea whether the experiments were correctly carried out or not, as Mr. Barkworth and Dr. Barclay had mislaid their notes and were unable to recall the suggestions they had given. Miss A. was roused from the hypnotic state and, as usual, remembered nothing of the suggestions. She was then re-hypnotised, asked to recall them, and replied as follows: "They were made at 4 p.m. last Wednesday week and were to be fulfilled in 21,400, 21,420, 21,428 and 21,434 minutes. Mr. Barkworth and Dr. Barclay gave two suggestions each." Miss A. stated that she had made no calculation at the time and had not thought of the suggestions afterwards. On April 22, Dr. Barclay sent me the lost memorandum of his two suggestions, viz., 21,428 and 21,434 minutes from 4 p.m. on the day already mentioned. On April 27, Mr. Barkworth wrote to tell me that he also had found his lost memorandum, and that the suggestions were 21,400, 21,420, 21,428 and 21,434 minutes, the first two having been made by himself, the two latter by Dr. Barclay. This agreed with Miss A.'s account.

A fresh series of suggestions was made on April 8, some to fall due during the night, others the following week in my presence. The patient lost her papers recording the former, and I was too busy to enter the latter. These are the only experiments in the whole series which are not recorded, and they are omitted for the above reasons. Later, Miss A. found the records of the suggestions, which had been carried out during natural sleep. They were correct.

Experiments, Thur., May 7, 3 p.m.—No. 50. *Sug.:* in 8,650 m.—No. 51. *Sug.:* in 8,680 m.—No. 52. *Sug.:* in 8,700 m.

I still further complicated these by suggesting as follows: "No. 50 is to be fulfilled in the waking state. Five minutes before No. 51 falls due you are to pass into the hypnotic condition. No. 51 is to be fulfilled during hypnosis, but five minutes afterwards you are to pass into the normal waking state and continue in that until after the execution of No. 52. Eight minutes after No. 52 is carried out hypnosis will again appear."

Results.—No. 50. (*a*) Suggestion fulfilled, Wed., May 13, 3.10 p.m. Correct. (*b*) Hypnosis appeared at 3.31 p.m. This ought to have been 3.35 p.m. and was therefore 4 minutes too early.

No. 51, Wed., May 13, 3.40 p.m. (*a*) Suggestion fulfilled during hypnosis. Correct. (*b*) Miss A. passed spontaneously into the normal state at 3.45. Correct.

No. 52, 4 p.m. (*a*) Suggestion fulfilled in the waking state. Correct. (*b*) Hypnosis appeared exactly at 4.8. Correct.

Remarks.—On May 13, Miss A. came into my consulting room at 3.5 p.m., and almost immediately fainted. She had recently met with a severe accident and was in acute suffering. Immediately on regaining consciousness she said she had to make a cross at 3.10, and did so in my case book; others were present in the room when all the suggestions were fulfilled with the exception of the first.

Experiments, Wed., May 13, 4.30 p.m.—The suggestions were given in the following general terms: "You are to repeat all the experiments made last Thursday, but to-day you are to start from 2.55 instead of 3 p.m., and to each suggestion you are to add 1,440 minutes." The original suggestions were not cited, nor any other information given. The experiments, therefore, were as follows:—

No. 53, Wed., May 13, 4.30 p.m. *Sug.:* in 8,650 m. from 3 p.m., plus 1,440 m., minus 5 m. from starting point.—No. 54, Wed., May 13, 4.30 p.m. *Sug.:* in 8,680 m. from 3 p.m., plus 1,440 m., minus 5 m. from starting point.—No. 55, Wed., May 13, 4.30 p.m. *Sug.:* in 8,700 m. plus 1,440 m., minus 5 m. from starting point.

Results.—No. 53, Wed., May 20, 3.5 p.m. Fulfilled in the waking state. Correct. Hypnosis appeared at 3.30. Correct. No. 54, Wed., May 20, 3.35 p.m. In hypnosis. Correct.

Miss A. passed spontaneously into the normal state at 3.40. Correct.

According to the original suggestions, Miss A. was to remain in the normal state until the fulfilment of the next experiment, but, as she had a severe headache, I hypnotised her, made curative suggestions, and told her hypnosis would terminate one minute before the next experiment fell due. She passed into the normal waking state at 3.49, six minutes too soon.—No. 55, Wed., May 20, 3.55 p.m. was written down at 3.50. Calculation, therefore, correct, but time appreciation 5 minutes too early.

I re-hypnotised Miss A. immediately the above experiment was fulfilled. At 4.3 p.m., while still in the hypnotic state, she said it was 3 minutes past 4, and that I had suggested that hypnosis would appear at that hour. This was correct.

Remarks.—It is to be noted that hypnosis appeared at 3.30 p.m., the exact time suggested. This is particularly interesting as the experiment, correctly executed at 3.30 on May 20, was the erroneously carried out experiment of May 13, complicated by five minutes having been deducted from its starting point and 1,440 added to its interval.

No. 55 was the last experiment of the series. A few others, similar in character, were made in October, 1896. These were successful but presented no fresh features, and as Miss A. had to cease her visits, owing to her approaching marriage, further experiment was impossible.

Summary.—Fifty-five experiments are cited; of these one, apparently, was either not carried out by Miss A., or unrecorded by me, while in another (No. 9) she mistook the original suggestion, but fulfilled it correctly in accordance with what she thought it had been. Forty-five were completely successful, *i.e.*, not only did Miss A. write down the correct terminal time, but this was done, also, at the moment the experiment fell due. Eight (Nos. 33, 38, 39, 40, 41, 46, 47, 55) were partially successful. In these the terminal time was correctly recorded in every instance, but there were minute differences, never exceeding five minutes, between the patient's correct estimate of when the suggestion fell due and the moment at which she carried it out. The proportion which these errors bear to their respective intervals varies between 1 to 2,028 and 1 to 21,420. The following table gives an analysis of the conditions under which the experiments were carried out and their results:—

Experiments.		Witnessed by				Results.		Unrecorded	Remarks.
		Friends or relatives.	Bramwell and others.	Bramwell alone.	Unwitnessed.	Correct.	Wrong.		
Fulfilled in the waking state	26	14	11	1	0	20	6	0	1 mistaken suggestion. 1 fulfilled 2 minutes too soon. 1 fulfilled 2 minutes too soon. 1 fulfilled 1 minute too soon. 1 fulfilled 2 minutes too soon. 1 fulfilled 5 minutes too soon.
Fulfilled in hypnosis	15	0	15	0	0	12	3	0	1 fulfilled 1½ minutes too soon. 1 fulfilled 2 minutes too soon. 1 fulfilled 1 minute too soon.
Fulfilled in natural sleep	13	0	0	0	13	13	0	0	In each instance figures which correctly represented the terminal time of the experiment were found at the subject's bedside in the morning, but there is no evidence to show whether this was done at the moment the suggestion fell due, *i.e.*, the subject's calculations were correct, but evidence as to time appreciation is wanting.
Unfulfilled ...	1	0	0	0	1	0	0	1	It is doubtful whether this experiment was carried out by the subject. It is, however, possible that I omitted to record it, as it fell due when I was engaged with another patient.
Total ..	55	14	26	1	14	45	9	1	

Similar experiments, more or less successful, were made with other somnambules, but in none were the results so striking as with Miss A. In those about to be cited the subject was Miss B., aged 20, an intelligent, well-educated girl, who had received some scientific training. Her arithmetical powers were superior to Miss A.'s, but she possessed no particular aptitude for appreciating the passage of time. She was a somnambule, could be rendered anæsthetic and analgesic by suggestion, and had been the subject of several painless minor surgical operations. Her health, from the commencement of the experiments to the present date (August, 1900) has been good.

The first experiments consisted in determining by suggestion the time of waking from normal sleep. The hours selected varied widely; but the results were almost uniformly successful and the greatest error recorded did not exceed five minutes. Others similar to Miss A.'s followed thus:—

Exp. 1, Nov. 25, 1895, 3.55 p.m. *Sug.:* in 24 h. and 50 m. *Res.:* Correct. *Remarks:* In reply to questioning in hypnosis, Miss B. stated that when the suggestion was given she calculated when it would fall due and determined to carry it out at that hour.—*Exp.* 2, Nov. 27, 1.20 p.m. *Sug.:* in 1,445 m. *Res.:* 10 m. too early.—*Exp.* 3, Dec. 6, 3 p.m. *Sug.:* in 1,440 m. *Res.:* Correct.—*Exp.* 4, Dec. 9, 3.15 p.m. *Sug.:* in 2,880 m. *Res.:* Correct.—*Exp.* 5, Dec. 12, 3.30 p.m. *Sug.:* in 1,540 m. *Res.:* 7 m. too late.—*Exp.* 6, Dec. 16, 3.30 p.m. *Sug.:* in 1,620 m. *Res.:* 13 m. too late.—*Exp.* 7, Dec. 20, 3 p.m. *Sug.:* in 1,380 m. *Res.:* Correct.—*Exp.* 8, Dec. 31, 3.15 p.m. *Sug.:* in 24 h. 1,200 m. *Res.:* Correct.—*Exp.* 9, Jan. 2, 1896; 3.10 p.m. *Sug.:* in 24 h. 1,430 m. Miss B.'s calculation, made in hypnosis, was 40 m. too early. *Res.:* 5 m. too late.—*Exp.* 10, Jan. 6, 3.15 p.m. *Sug.:* in 24 h. 100 m. Miss B.'s calculation in hypnosis was correct. *Res.:* 8 m. too late.—*Exp.* 11, Jan. 27, 3.10 p.m. *Sug.:* in 24 h. 150 m. Miss B.'s calculation in hypnosis was correct. *Res.:* 10 m. too soon.—*Exp.* 12, Mar. 27, 3.10 p.m. *Sug.:* in 24 h. 240 m. Miss B.'s calculation in hypnosis was correct. *Res.:* Correct.

Time experiments more or less closely resembling those cited have been occasionally repeated with Miss B. up to the present date (August, 1900) and with practically identical results.

Before considering theoretical explanations of hypnotic and post-hypnotic appreciation of time, I propose to discuss (*A*) the possibilities of mal-observation or deception, and (*B*) to draw attention to certain other points which appear worthy of notice.

(*A*) *The Question of Mal-observation or Deception.*

(1) The subjects of all my time experiments were either former patients or personal friends. None of them were trained hypnotic subjects, and in no single instance was a pecuniary reward promised or given. All this, however, does not in itself exclude the possibility of mal-observation or deception, and I would rather base my arguments in favour of the genuineness of the results on post-hypnotic amnesia, and the fact that the problems involved were beyond the subject's waking powers.

(2) While, however, all observers recognise post-hypnotic amnesia, it must still be admitted that loss of memory might be assumed for purposes of deception. Fortunately, there are other hypnotic phenomena impossible of imitation; amongst these may be cited: (*a*) the absence of certain organic changes following injury (Delbœuf's case of two symmetrical burns), and (*b*) the absence of physiological signs of pain during severe and prolonged operation. The latter fact was clearly demonstrated in the operations on my patients at Goole and Leeds (*Journal of Dental Science*, March 30, 1890, and *Lancet*, April 5, 1890). Several of these patients were afterwards the subjects of my time experiments, and all who were employed for this purpose, including Miss A. and Miss B., could be easily rendered anæsthetic or analgesic by suggestion.

(3) Post-hypnotic amnesia alone, even when it is undoubtedly genuine, does not exclude possible error, as the subject might receive information from the operator or spectators. It is, however, difficult to say how this could have happened in Miss A.'s case. Thus, twenty-seven experiments were fulfilled in my absence, and no information regarding these—excluding, of course, the suggestions

made to Miss A. during hypnosis—was given to anyone until some time after the whole series was completed. I did not calculate when any of these twenty-seven suggestions would fall due, and did not know, until after their fulfilment, whether they had been carried out correctly or not. Twenty-seven further experiments were fulfilled in my presence, these, with one exception, were also witnessed by others. In four of them the suggestions were made by Mr. Barkworth and Dr. Barclay, and I did not know what they were until afterwards. These two operators, however, could not assist the subject, as they had lost the memoranda of their suggestions and were unable to recall the figures. In the remaining twenty-three, none of the spectators knew what the suggestions were. Indeed, in most instances, they did not know that any experiments were being carried on, until they saw them executed and were asked to witness the figures, their ignorance being purposely arranged.

(4) In the twenty-three cases just cited, before giving the suggestions, I calculated when they would fall due. Could Miss A. have learnt anything about this through telepathy or muscle-reading? During the last ten years, I have searched for evidence of telepathy and also taken part in the experiments of other observers; the results, however, have invariably been negative; if, for argument's sake, we conceded the possibility of telepathy, recognising that somnambules possess hyperæsthesia of the special senses, it would still be difficult to see what information Miss A. could have obtained from me. In the majority of the experiments I did not work out when the suggestions would fall due, and even when I did, many of my calculations were only approximately correct, although I was not aware of this until after all the experiments were completed. Moreover, I I have an unusually bad memory for figures, and never either before or during the execution of the suggestions, recalled my calculations as to the time at which they were supposed to fall due. Further, when the experiments were carried out I was nearly always busily engaged with other patients and so placed that Miss A. could not see my face.

(5) Again, even supposing post-hypnotic amnesia had

not existed in Miss A.'s case, the retention in the waking state of the memories of hypnotic life would not in itself explain her feats in calculation and time appreciation. Miss A.'s memory, knowledge of arithmetic and power of appreciating time, in no way exceeded that of other imperfectly educated girls in her station of life. Her normal memory was incapable of retaining complicated series of figures, and she was unable to make even much simpler mental calculations than those involved. After the suggestions were made, she remained in the hypnotic state for an hour or more and could not consult the clock. During this period it was absolutely impossible for her to record the suggestion in any way other than mentally.

(B) Other Points of Interest.

(1) Five minutes before the first experiment was fulfilled, Miss A. became restless and felt she must do something. This preliminary stage of restlessness was absent in all the others. In them, when the time for carrying out the suggestions arrived, Miss A. had a sudden twitching of the fingers of her right hand, immediately followed by the idea of writing down certain figures. The abruptness of this invasion of the normal consciousness, by a message from the subliminal one, was particularly noticeable when Miss A. was actively engaged in conversation at the time.

(2) On twenty-four occasions Miss A. was asked to calculate when the suggestions fell due; she was wrong in the first nine instances, but in the remaining fifteen right in eleven and wrong in four. As the experiments advanced, not only the frequency, but also the extent of Miss A.'s errors in calculation decreased, and the answers were given much more rapidly. Sometimes the correct replies were almost instantaneous, and in these instances no conscious calculation could be traced. It is to be noted that Miss A.'s mistaken calculations had no effect on the correctness of her results.

(3) *Memory.*—Once only did Miss A. spontaneously recall in hypnosis that a time suggestion—yet unfulfilled—had

been given. This was *Experiment No.* 3, where the suggestion was an easily remembered one, viz., 24 hours and 100 minutes. On other occasions when Miss A. was questioned in hypnosis as to the unfulfilled suggestions, she invariably recalled the fact that these had been made, but rarely remembered their exact terms. She always asserted that she had never thought of them, did not know how much time had elapsed since they had been given, nor when they were due. This was so even in cases where she had calculated the terminal time. At first Miss A. forgot all about the suggestions immediately after they were fulfilled; she did not know she had made a cross or written down the figures, and could not recall what they meant. This condition of memory was identical with what is almost universally associated with post-hypnotic acts. Later, for convenience' sake, it was suggested to Miss A. during hypnosis that she should remember having executed the experiments. She then knew in the waking state that she had made a cross and written down certain figures, but recalled nothing of the original suggestion, of which these acts were the fulfilment. When Miss A. was questioned in hypnosis, after the execution of the suggestions, her memory, on certain points, was very clear. She could recall in every detail the terms of all experiments that had recently been carried out, *i.e.*, she remembered the hours at which they had been made, the number of minutes suggested, her own calculations, if any, and the moment and circumstances under which the suggestions had been fulfilled. Putting aside the calculations she made at the time, in response to suggestion, she was unable to recall having made any others, or to give any information as to the methods by means of which she had correctly fulfilled the experiments. When a second series of suggestions was given, before the first had been fulfilled, after all had been carried out, she could recall both series and place each member of them in its proper order. This memory, however, was not persistent. A fortnight after the experiments had been executed, although Miss A. still remembered in hypnosis that they had taken place, she was unable to recall the details. When experiments were fulfilled in normal sleep she remembered their terms in hypnosis and when they had been given, but not when they had been executed.

(4) The experiments had no prejudicial effect on Miss A.'s health. On the contrary, this steadily improved. She is now a strong, healthy, well-developed woman, the mother of two children, and has had no return of her nervous symptoms.

In no single instance did any bad effect, even of the most trivial description, follow hypnotic experiment.

(5) The results of the experiments were only estimated after the series was completed, when a friend, Mr. Bartrum, B.Sc., kindly checked them for me. He discovered that some of my calculations made at the time had been erroneous. I am also indebted to him for a critical examination of the calculations the patient was asked to make when the suggestions were given.

(6) With the following exception, the phenomena observed in the cases of Miss A. and Miss B. differed little. When a simple suggestion was given, Miss B. sometimes spontaneously calculated when it would fall due. Miss A., on the other hand, never made any spontaneous calculations at all. Apparently Miss B. did not spontaneously calculate the more complicated arithmetical problems. When she did so, in response to suggestion, her results were invariably correct, but, despite this, the experiments were not always fulfilled at their appropriate time. Miss A., on the contrary, was often wrong in her calculations, while the suggestions themselves were carried out with phenomenal accuracy.

(7) In some recent instances Miss B. apparently made no spontaneous calculations, despite the fact that the arithmetical problems involved were extremely simple. For example, I suggested that she should shake hands with me forty minutes after I aroused her from hypnosis. At the moment indicated, in the midst of an animated conversation, she suddenly asked me to shake hands with her. In reply to my questions, she said she had felt impelled to do this, but could not tell why. A few minutes later she had entirely forgotten the incident. I re-hypnotised her; she then re-

called the suggestion and the impulse she had experienced, but could not remember having made any calculation or having in any way marked the passage of time.

THEORETICAL EXPLANATIONS.

Delbœuf, as we have seen, pointed out that the terminal day in Beaunis and Liégeois' experiments fell on an easily recognised date with which the subjects were acquainted. These experiments, he said, did not show, as they were supposed to do, that somnambules possessed the power of counting days, but only that they were able to retain a given date. To remove this objection his suggestions were made in minutes, while the majority of mine were given in a similar but even more complicated form. In explaining the phenomena, therefore, we must take into account, not only the appreciation of the passage of time, but also the feats of memory and arithmetical calculation which sometimes exceeded the subject's normal powers.

Bernheim's Theory.

This is mainly based on the supposed occurrence of self-hypnosis in somnambules and the existence during that condition of a peculiar mental concentration, with consequent revival of hypnotic memories. According to Bernheim, conscious mental activity exists both in sleep and in hypnosis. During sleep we are conscious that our mind thinks and works, just as the somnambulist knows what he is doing, but the form of consciousness differs from that of waking life. In both, concentration of the nervous force upon the suggested image or idea is the characteristic phenomenon. This continues to exist, although dream succeeds dream in sleep and varying suggestions are instantly executed in hypnosis; the nervous concentration has only changed its object, the focus shifted its place.

According to Bernheim, if an individual goes to sleep determined to wake at a given hour, his attention is fixed upon this idea, and he thinks about it voluntarily and consciously all night. When he awakes, he believes he has done so spontaneously, as the conscious thoughts of sleep are forgotten. Finally, he says, the lost memories of hypnosis may be revived by chance association of ideas, like forgotten impressions of the waking state, and also in other ways, and thus, the memory of the suggestion has not been latent all the time. In support of this he cites :—

First—*Experiments.*—Two subjects, who had received deferred suggestions, when hypnotised and questioned in the interval, stated that during natural sleep they had once dreamt of what had been suggested during hypnosis.

Secondly—*Certain general observations as to the mental condition in somnambules.*—The memory, he says, of what has taken place during hypnosis depends upon the psychical concentration already referred to; every time this is reproduced, the lost memory is revived. Somnambules pass easily and spontaneously from the normal to the hypnotic state; they then become self-absorbed and concentrated, and recall the operator's suggestions. They know when these should be executed and take their measures accordingly; they reinforce the idea of not forgetting them, just as a person in natural sleep determines not to miss the hour set for waking. Although the suggestion may have been present in their minds the greater part of the day, they forget this if we divert their attention from themselves by speaking to them. By doing this, we have disturbed their psychical concentration, drawn their cerebral activity from the inside to the outside, and produced another state of consciousness in which the memory of the suggestion is lost; the memories of the second, or hypnotic state, being effaced in the first, or normal, one.

In consequence of this, when the somnambule carries out a suggestion, he believes that the idea has newly and spontaneously dawned in his mind—"*He no longer remembers that it is a memory.*" Thus, in Bernheim's opinion, a deferred suggestion is no more difficult to explain than one executed immediately on waking.

Three points are involved in Bernheim's theory.

(1) *Nervous concentration and its relationship to hypnotic memory.*—According to Bernheim, everyone possesses a certain definite amount of nervous force or cerebral activity. In the waking state this is concentrated in the higher nervous centres — the reasoning part of the brain; in hypnosis in the lower ones—the imaginative or automatic part. All the phenomena induced during hypnosis—conceptions, movements, sensations, images—owe their origin to this concentrated and accumulated nervous force. When the subject passes into the normal state this nervous concentration ceases, and the impressions received during hypnosis fade. When hypnosis is again induced, the former state of concentration reappears and, at the same time, the lost memories are revived.

This explanation is ingenious, but not in keeping with observed facts. If I suggest to a subject that he will still remember the events of hypnosis, after that state has terminated, he invariably does so. Yet, according to Bernheim's theory, the redistribution of nervous force to the higher centres should inevitably have prevented this. Again, suggestion may rob the hypnotised subject of the power of recalling the events of previous hypnoses. If, however, Bernheim's explanation be correct, the lost memories could not escape revival, seeing that they must have reappeared when the nervous force was again concentrated in the lower centres.

Further, as numerous and varied hypnotic phenomena can be simultaneously evoked in the same subject, this clearly shows that the phenomena of hypnosis cannot be explained by the concentration of attention on any one given point. Again, the fact that the multiple phenomena are sometimes similar in character to the isolated ones, indicates that the explanation of hypnotic phenomena by means of the amount of attention concentrated is also fallacious. If all the attention is requisite for the production of one hypnotic phenomenon and yet, while it still lasts, many others are simultaneously induced, whence do these derive that excessive amount of attention which is said to be necessary for the induction of the primary phenomenon?

(2) Admitting that hypnotic memory is associated with this psychical concentration, the evidence in favour of the frequent and spontaneous occurrence of the latter is far from convincing. Granting that two subjects had each *once* dreamt of a suggestion during natural sleep, this does not justify the conclusion that somnambules pass easily and spontaneously from the normal to the hypnotic state. Further, although the memories of hypnosis, whether self-induced or not, are lost on waking, these can be easily evoked by questioning in subsequent hypnoses. If, therefore, subjects passed spontaneously into the hypnotic state, and thought about the suggestions, they could be made to recall the fact that they had done so. Despite this, Bernheim's generalisations are founded on the two dreams just cited; and he has apparently made no attempt to discover the actual mental conditions involved, although he might easily have done this by means of the simple method of interrogation in subsequent hypnoses.

(3) Granting both the points in dispute, *i.e.*, the psychical concentration and its spontaneous occurrence, the difficulty is still unsolved. If no trace of the hypnotic memory remains in the normal state, what advantage does the normal consciousness obtain from the unknown or forgotten fact that the hypnotic consciousness recalled the suggestion at some time before the date fixed for its fulfilment?

Beaunis' Objections.

Beaunis also raises many objections to Bernheim's views. Thus, while admitting the influence of attention and concentration upon the production of certain hypnotic phenomena, he holds that these are insufficient to explain deferred suggestions. They may account for a hallucination realised immediately on waking, but not for one that has been retarded for several days. Here, the subject was unconscious of the suggestion until the hallucination appeared at the hour fixed, and it is absurd to suppose that all this time he was under the influence of a dominant idea. Bernheim's experiments, therefore, do not settle the question.

Granting that the subject dreamt of the suggestion in normal sleep two days before it fell due, it is still necessary to explain how it was carried out at the time fixed. The suggestion, it is true, now involves a shorter period of time, *i.e.*, two days instead of the original number, but this, while reducing the extent of the problem, still leaves it unsolved.

Beaunis disputes Bernheim's assertion that those who wish to wake at a given hour think of this all night, for, he says, if this were true, they would afterwards remember having done so. Dreams which have passed rapidly through the brain can often be recalled in every detail; we should, therefore, be able to remember still more vividly the ideas upon which our attention has been continuously fixed. Further, some people always know what o'clock it is, and, if suddenly asked, are able to give an exact reply, no matter how much their attention may have been concentrated on other things. Had they consciously noted the passage of time, they would afterwards be able to recall having done so. This, however, is not the case, and they are unable to explain how the feat was performed.

Finally, in contradistinction to Bernheim, Beaunis justly points out that important differences exist between the way in which the lost memories of the waking state and those of hypnosis are revived. The former may be recalled at any time by a chance association of ideas. For example, things long forgotten may be remembered on hearing the name of someone we knew in childhood. The lost memories of hypnosis, however, possess the distinctive and essential characteristic that they cannot be revived by a chance association of ideas, and are, therefore, fundamentally different from those of the waking state. The hypnotic suggestion is only realised at the hour fixed and cannot take place before, even when associations occur which would have restored lost normal memory. Thus, if it is suggested to A. that he is to do something at the expiration of ten days, when he hears B. cough three times, B.'s signals, if given at any time before the day fixed, produce no response, although they inevitably do so when the appropriate time arrives.

Beaunis' Theory.

Beaunis attempts to explain the phenomena of time appreciation by the existence in the human organism of an unconscious physiological power of time measurement. The phenomena of deferred suggestion, he says, is analogous to that of awaking at a fixed hour from normal sleep, and both may be explained by the existence of a sort of mental mechanism, arranged, like an alarm clock, to produce a movement at a fixed hour. The brain is a machine which acts without our knowledge, with an activity we are unable to estimate, and the things of which we are conscious only feebly represent this mysterious work. The power of appreciating time, rudimentary or rather atrophied in civilised man, is well developed in the savage and lower animals. Thus a dog, accustomed to go out with his master at a certain hour, will show that the time has arrived by expressive pantomime, should his master delay a little in getting ready for his walk. In Beaunis' opinion, the measurement of time by somnambules is an act of unconscious cerebration.

Paul Janet's Objections.

Janet grants that an image of which one is unconscious may exist in the memory, and, further, that it can be revived, even at a fixed date, if the operator associates the suggestion with some definite sensation, as, for example, the sight of a particular person. He cannot, however, understand the return of the lost memory at a fixed day, without other association than the numeration of time. Thirteen days, for example, do not represent a sensation, but form an abstraction. The carrying out of a suggestion, therefore, at the expiration of such a period, presupposes the existence of an unconscious power of measuring time—an entirely unknown faculty. Up to this everything could be explained by the law of association of ideas; but here we make a sudden jump, and the thread of analogy is completely broken. No association can explain the unconscious counting of thirteen days, and the "suggestion theory" is in default.

Beaunis' Reply.

A day is not an abstraction. The idea of a day represents a series of definite impressions, the result of external agencies, such as light, temperature, &c., which produce in our organism different kinds of reactions. A day is, then in reality, not a sensation, but a succession of sensations and unconscious reactions. Animals know exactly the hour at which they are habitually fed, and an attack of fever returns at the same hour each day, or every other day, for weeks; this indicates that the measurement of time is not an abstraction, but has its roots in the very life of the organism. The periodicity of days, weeks, months and seasons corresponds to periodic organic variations, which under certain circumstances might acquire sufficient intensity to constitute a sort of "unconscious faculty for measuring time," although the word "faculty" is a little too philosophic a term for an organic aptitude of this kind.

Remarks:

Beaunis' explanation assumes (1) the existence of an unconscious faculty for measuring time, and (2) its applicability to the cases in question.

(1) *The unconscious measurement of time.*—According to Beaunis, time appreciation is highly developed in savages, while certain civilised persons can awake at a given hour, and others always know what o'clock it is. In support of this, however, he does not cite a single example or experiment. Let us take the simplest case, *i.e.*, waking at a given hour. Many persons, it is true, believe they can do this; usually, however, the self-waker only shows the power of giving himself a lighter sleep than usual; he wakes several times during the night, and, in the end, does not always hit the exact hour. On behalf of the Society for Psychical Research, several persons, who believed they possessed this power of self-waking, tested it in a rigorously scientific manner. The results were disappointing. One experimenter only succeeded on two occasions out of seventeen, and one of these was his usual hour of waking; another was successful on five times out of twenty-nine, but on three of these he

awoke at other hours as well, while the third was right two out of thirteen times, and the fourth succeeded in four instances out of forty-six.

Since I became interested in time appreciation, many people have assured me that they could awake at any given hour. None of them, however, were able to experimentally reproduce the alleged phenomenon, while the two following are the only genuine cases I know of:—

Dr. George Savage possesses the power of waking at a given hour and has tested it on many occasions. The following is an example:—One day, having to catch an early train, he determined to wake at 6 a.m., and slept soundly without waking until the exact time. The seven following mornings he woke exactly at six, notwithstanding that he went to bed at different hours, and there was no necessity for early rising. This involuntary repetition of self-waking at unusual times also occurred when he was roused by others at abnormally early hours. Thus, when in the Alps, if he were called at 2 or 3 a.m., he would certainly wake spontaneously at the same hour next morning, even if he had been much fatigued with climbing. Dr. Savage states that the accuracy of the time of waking in these instances has puzzled him greatly.

The following is Professor Marcus Hartog's own account of his case:—

"When I was a student, under 17, I found I could, sleeping soundly, awake at any given time I had set myself overnight. The peculiarity of such waking was that it was always sudden and complete, not preceded by a period of light broken sleep, nor accompanied by the drowsiness of an ordinary unprepared waking. If I found that it was needless to get up I soon fell asleep again, and then had the ordinary drowsy waking, often oversleeping myself. This faculty has persisted with me. Between the ages of 20 and 25, on three distinct occasions I had to nurse friends, when I had to administer food and medicines at regular intervals, as well as to attend to every call or unrest on the part of the patient. The last occasion extended over, I think, three weeks. On each occasion the facility and manner of waking completely and suddenly was exactly the same as for early rising, whether at the stated call, or at the least stir of the patient. On lying down to rest again I seemed to see a gradually widening vista, and as my eyes diverged I fell asleep; the time occupied could not have been a quarter of a minute, though I felt wide awake at the moment of closing my eyes. My sleep on these occasions was singularly if not absolutely dreamless, though I was under the greatest mental anxiety while waking."

In Professor Hartog's case the waking at fixed hours was never involuntarily repeated, *i.e.*, as regards the waking at repeated intervals. Sometimes, however, when he set himself to wake at a fixed time in the morning this was repeated for several days, as in Dr. Savage's case.

(2) *The applicability of Beaunis' theory to the particular cases in question.*—The experiences of Savage and Hartog undoubtedly show that certain persons can wake at a given hour. This does not, however, explain why this power is almost universal amongst somnambules; it is an attempt to explain the little known in terms of the less known, and the analogy, even if successfully established, does not solve the problem but adds another to it. Granting that the uncivilised man possesses some natural power of marking the passage of time, it would be of little use to him in cases such as those cited by Delbœuf and myself. If he cannot count above five how is he to bring his powers to bear on a suggestion which starts from, say, 3.15 p.m. yesterday and is to terminate in 20,840 minutes?

Delbœuf's Theory.

Delbœuf first pointed out that his subjects in the normal state were unable to make the necessary calculations involved in his time experiments. As the latter were successful this showed, he said, that the subjects, when hypnotised, had an idea of the passage of time and unconsciously calculated when the suggestions fell due. Apparently they possessed a sort of mechanism like an alarm which they set to go off at a fixed time.

Edmund Gurney's Objections to the Theories of Delbœuf and Beaunis.

According to Gurney, commands to be fulfilled at a particular date involved the reckoning of time. This was usually assumed to be physiological. Thus, Delbœuf believed that the subject calculated when the order fell due, and said to himself: "I shall fall into a trance at such and such a moment and then perform the act." The subject set his organism like an alarm for a given time ahead; his mind, relieved of responsibility, then went off duty till the suggestion fell due, when it was aroused by its own automatic machinery, the action resembling the running down of an alarm. Gurney asserted that hypnotic subjects never formulated their orders in this way, and that Delbœuf's explanation was pure guess work, unsupported by fact.

Further, he said, even if we granted the purely physiological hypothesis for cases of short duration, where the idea of the time fixed could be easily grasped, and thus the setter of the alarm knew exactly what he was about—it would be a very different thing to extend it to others where the command had been executed after the lapse of months.

Gurney, like Delbœuf, drew a distinction between commands to be carried out at a specific date, such as New Year's Day, and those where the length of time alone was named, as in the direction to do something "on the 69th day from this." In the former instance the brain might at once register the date along with the order, and the arrival of the former would thus suffice to arouse the latter. A length of time could not be registered in this way. Its termination, till reckoned by the calendar, was quite indefinite, and when the particular day arrived it conveyed nothing likely to revive the suggestion—it carried no more *sixty-ninthness* about it than any other day.

Gurney considered that Beaunis' explanation did not fully meet Janet's objection that such a length of time—*i.e.*, 69 days—was simply an abstraction. Admitting that "a day" was a sufficiently familiar and definite unit to present a concrete character, that it represented a series of conscious reactions, and, further, that there were periodic organic changes which extended over weeks and months, this did not prove that "the measurement of time was not an abstraction, but had its roots and conditions in the very life of the organism." It did not follow that "sixty-nine days" were concrete in character because this was the case with "one day," and, further, the organic conditions associated with established physiological periods were absent from those suddenly and arbitrarily fixed by human volition. The vital processes were as unable to make a time calculation of this kind as a school boy's digestion to work out a proposition of Euclid. Such time measurement was not a function of animal life; its result was not an inevitable bodily state, but a needless act. It depended—not on progressive changes in the stomach or blood—but on an original course of cerebration taking place in the higher tracts of the brain, initiated by an impression—that of the command—which had a distinct psychical side.

According to Gurney, the passage of time must be registered, looking at it from the brain side alone, not by general gradual change, but by a series of specific changes corresponding to the days and units of measurement, and this was the only kind of cerebral process capable of clearly differentiating the case from that of ordinary physiological time reckoning. Further, unless cerebral events such as were normally correlated with the ideas "sixty," "sixty-one," "sixty-two," &c., really took place, how could the gulf be spanned with precision? Any other kind of change would not know when to stop, or how to associate a point it had reached with the order given long before. Granting that these specific brain-changes took place, was it not reasonable to suppose that their mental correlate existed; and that, hidden from our view, there was an actual watching of the course of time? This hypothesis went a long way towards removing Paul Janet's difficulty. From this point of view his "unknown faculty" resolved itself into a known one, working in the normal way, but below the surface of ordinary consciousness.

Gurney's Theory.

As we have seen, the carrying out of a post-hypnotic command several thousand minutes after waking can neither be explained by any ordinary physiological power of appreciating time, nor by a supposed spontaneous re-hypnosis with temporary revival of memory. The feat, according to Gurney, can only be performed as the result of the intelligent action of a secondary consciousness, which watches the time as it passes just as the ordinary one would do, and, when the correct hour arrives, pushes the ordinary consciousness on one side, takes its place and carries out the command. In Gurney's opinion, the mental conditions involved in the execution of post-hynotic commands varied widely in different cases. Of these the following are examples:—

(1) A subject was told to do something ten minutes after she awoke. On waking she looked at the clock until the expiration of the time, then executed the order. In this case, the subject was conscious of having consulted the clock, and afterwards—apart from any question of the revival of hypnotic memory in post-hypnotic states—remembered having done so.

(2) A subject was told to do something five minutes after he awoke. Immediately on waking he looked at the clock and continued to do so at intervals, talking naturally meanwhile to those present. At the end of five minutes he executed the order. Afterwards, he neither recollected looking at the clock, nor carrying out the command.

This case appears to occupy an intermediate position between No. 1 and the others about to be cited.

(3) A subject was told that on the 39th day from then he was to execute a post-hypnotic suggestion. He had no memory of the command when awake, and no reference was made to it until March 19, when he was suddenly asked, during hypnosis, how many days had elapsed since it was given. He instantly replied, "Sixteen," and added that there were twenty-three more to run. Both statements were correct.

(4) Another subject was told on March 26, that he was to do something on the 123rd day from then. On April 18, he was hypnotised and asked if he remembered the order. He at once replied: "Yes, this is the twenty-third day; a hundred more." Further questioning made it clear that every few days the command occurred to his mind and that

he calculated how many days had passed and how many more had to elapse. His waking memory retained no recollection of the original suggestion, nor was it aware of the memories and calculations which he described when hypnotised.

In the two last cases, the watching was undoubtedly wholly of an internal kind, and, although obviously accompanied by consciousness, was afterwards entirely forgotten.

The two points in Gurney's theory which specially demand consideration are: (I.) What evidence have we of the existence of a secondary consciousness? (II.) Granting its existence, how far does it explain all the phenomena we have been considering?

(I.) *The secondary or subliminal consciousness.*

The facts in favour of the existence of a secondary consciousness may be divided into three groups: (*a*) Those arising from, or more or less closely associated with, morbid states; (*b*) Those occurring in normal waking or sleeping life; (*c*) Those arising spontaneously, or as the result of suggestion, in the hypnotic condition.

(*a*) To those who have not studied hypnotic and cognate phenomena, this group is practically the only one that exists. Its most familiar examples are to be found in post-epileptic and other more or less clearly defined morbid conditions. Here the personality of the secondary consciousness is generally a reduced one; volition is frequently suspended or weakened, and consciousness dimmed. The individual does not recognise himself, his surroundings and mental state, in as clear a fashion as he would do were he in his normal condition.

The case of Louis V. is one of the most interesting of this kind. This young man presented two distinct mental, moral, and physical states. In the primary, he was docile and intelligent, while sensibility and movement were normal. In the secondary, he was violent, vicious, less intelligent, and presented hysterical contractures. Each state was completely independent of the other and possessed absolutely distinct memories.—"The Life History of a Case of Double or Multiple Personality," by A. T. Myers, M.D. (*Journal of Medical Science*, January, 1896); "Les Variations de la personnalité," par MM. Bourru et Burot (*Revue de l'Hypnotisme*, 1887, p. 193).

Dr. Rieger (*Der Hypnotismus*, 1884, pp. 109-115) cites a case of frequently recurring attacks of secondary consciousness in an epileptic. In the normal condition his character was orderly, but this state alternated with others during which he would leave his home for weeks at a time and lead the life of a thief and vagabond, sometimes being sent to prison, sometimes to asylums. In his primary condition, he had no memory of the acts for which he had been punished.

Dr. Lewis C. Bruce (BRAIN) gives an account of an asylum patient who not only showed two separate and distinct states of consciousness, but in whom the right and left brain alternately exerted a preponderating influence over the motor functions. At one time he was ambidextrous and only understood English, at another he was left-handed and spoke Welsh.

Spontaneous somnambulism affords another example of the action of a secondary consciousness. In volition and consciousness are to be found the main differences between it and induced somnambulism. The hypnotic subject knows what he is doing and why he does it, and can reject disagreeable suggestions. Unless specially trained, he usually only acts in response to influence from without—influence more or less directly transmitted to him by the suggestions of others. The spontaneous somnambule, on the contrary, acts his own dreams. His hallucinations sometimes excite criminal acts, and authentic cases are reported in which spontaneous somnambules have committed murder, under the delusion that the person they attacked was a wild beast or a burglar. Spontaneous somnambulism, properly speaking, is a neurosis, and, as Hack Tuke pointed out, in its severest forms approaches perilously near epilepsy, while the condition of mental automatism which sometimes succeeds epileptic fits closely resembles that of the sleep-walker. Yellowlees looks upon spontaneous somnambulism as a form of insanity, and calls it *somnomania*. He holds that the sole difference between it and insanity or epileptic violence is that it occurs during sleep, and involves only a temporary arrest of volition, instead of the more prolonged loss of control which results from organic mischief.

In another group of cases the secondary state, while markedly inferior to that particular individual's primary one, finds its counterpart in degenerate states which are not necessarily insane.

Of this the following case, recorded by "Dagonet" (G. R. Sims) in the *Referee*, January 31, 1897, is an example:—One night Mr. Sims received a message from the master of a workhouse, to the effect that the police had brought a man to the infirmary whom they had found insensible in the street, apparently suffering from drink; a letter, signed by Mr. Sims, was in his pocket. Mr. Sims knew him as a professional man in a good position. Next day he was conscious, but absolutely denied his identity. He said he was a street musician, and that his cornet had been stolen during a row in a public house where he was playing. He returned to his lodgings as soon as he was discharged from the infirmary, and told his landlady he thought he must have had a fit and fallen down in the street, for he was bruised and ached all over, but did not remember anything about it. Exclusive of the time passed in the infirmary, he had been absent from his lodgings a week, but maintained that he had only left the house that morning. A few days later he fulfilled an important professional engagement. All went well for some time, then he again suddenly disappeared. Search was made for him, and he was eventually found playing a cornet outside a public house in Camden Town. Addressed by his proper name he made no sign, and when questioned asserted that he had been an itinerant musician for the last fifteen years. To-day Mr. —— is again living an ordinary respectable professional life, and has not the slightest knowledge of his periodical lapses into another individuality—that of a street musician. His name is well known to all who are familiar with music and the drama.

In another group, the secondary state, instead of being one of obvious mental disorder, differs little in intelligence and volition from the primary one. The following are examples:—

Ansel Bourne, an itinerant preacher, aged 61, residing at Greene, Rhode Island, suddenly disappeared. In spite of the publicity which the newspapers gave to the fact, and the efforts of the police to find him, he remained undiscovered for two months. He then found himself at Norristown, Pennsylvania, where for the previous six weeks he had been keeping a small variety store under the name of A. J. Brown, appearing to his neighbours and customers as a normal person. When his normal consciousness returned, he was extremely alarmed to find himself in an unknown situation, with absolutely no memory of his surroundings, or of the incidents which had taken place from the date of his disappearance.—*Proceedings of the Society for Psychical Research*, 1891, p. 221.

Emile X., barrister, sometimes passed, without loss of consciousness, into a secondary condition, which lasted from a few minutes to several days. During it he led an active life, which apparently did not differ from his normal one. The state always terminated suddenly, and the ordinary consciousness retained no recollection of what had just passed. After one attack, which lasted three weeks, he came to himself a hundred miles from home.—Dr. Proust, Professor of Hygiene at the Hôtel Dieu, Paris. *Revue de l'Hypnotisme*, March, 1890.

Mr. N., aged 32, educated, consulted Forel and told him the following story. He stated that he had been living for some weeks in Zürich, and had vague recollections of arriving there after a long voyage. Recently he had read two newspaper notices describing the sudden disappearance from Australia of a Mr. N., and he felt that he was the person referred to, although at the same time it seemed impossible that this could be true. N. entered the Burghölzli Asylum for treatment and was hypnotised by Forel, who succeeded in restoring his lost memory by suggestion, and thus obtained an account of his doings from the time he had left Australia. There was no reason, pecuniary or moral, for N.'s disappearance. He recovered under Forel's treatment.—*Ein Fall von temporäner, totaler, theilweise retrograder Amnesie (durch Suggestion geheilt)*, von M. Naef, Voluntärarzt an der Heilanstalt Burghölzli. *Zeitschrift für Hypnotismus*, 1897, p. 321.

The following is the most recent example I have been able to trace of the group we are considering:—On April 16, 1900, George Ridderband, aged 19, a law student and the son of a well-known lawyer, suddenly disappeared from his home in New York. No reason, except that he had been studying hard for an examination, was discovered for this, either at the time or afterwards. His parents put the matter in the hands of the police. On April 21 the lad walked into a police station and told the following story:—Five days previously, he suddenly found himself walking in the street, but neither knew who, nor where he was, nor could he recall anything as to his past life. Since then he had been wandering about, struggling in vain to revive his lost memories, keeping meanwhile a diary of his proceedings. He asked if anyone corresponding to him had been advertised as missing, and the sergeant recognised him as the lost George Ridderband. He was taken home and placed under medical care. At first he did not recognise any of his relatives, but a week later his memory commenced to return; he was still, however, unable to account in any way for his disappearance.

In another group the secondary state, from a physical, moral and intellectual point of view, is superior to that of the primary one. The following are examples :—

A girl, aged 18, healthy, but quiet and somewhat stupid in character, swallowed some unguentum lyttæ. After the acute symptoms of poisoning passed off, a cutaneous hyperæsthesia of the head and morbid sensitiveness to sound remained. She had frequent attacks of temporary insensibility and passed alternately from her ordinary mental condition to a secondary one, and from this in its turn back again to the normal one. In the secondary state she was excitable; her conversation was lively and spirited, and she was intellectually superior to what she was in the primary condition. The memories of the two states were absolutely distinct; the primary self knew nothing of the secondary one, the secondary self nothing of the primary one.—" Case of Double Consciousness," by Thomas Mayo, M.D., F.R.C.S., *London Medical Gazette*, New Series, Vol. I., 1845, p. 1202.

Mary Reynolds, a dull and melancholy young woman, was found one morning in a profound sleep, from which it was impossible to arouse her. After twenty hours she awoke, but her disposition was absolutely changed and she had no memory of her past. She was now cheerful, buoyant, sociable and merry, but did not recognise her relatives or friends, and had lost the power of reading and writing. Five weeks later, she passed into the primary state; again became dull and melancholy, and remembered nothing of her secondary condition. After the lapse of a few more weeks she again passed into the secondary stage after a profound sleep, and took up her new life precisely where she had left it. The memories of the two states were absolutely distinct; in the first she remembered former primary states, but these alone, in the second, she only remembered former secondary states. These alternations of consciousness continued for fifteen years, then finally ceased, leaving her permanently in the second state. In this she remained without change for the last twenty-five years of her life.—" Case of Mary Reynolds," by Dr. Weir Mitchell. *Trans. of the College of Physicians of Philadelphia*, April 4, 1888.

Félida X., aged 14½, without known cause, though sometimes under the influence of emotion, had attacks of sharp pain in both temples, followed by a state of profound stupor, which lasted ten minutes. She then spontaneously opened her eyes and appeared to wake, but in reality passed into a condition of secondary consciousness. This lasted for an hour or two, then the stupor and sleep re-appeared and she passed into her ordinary state. The secondary state differed markedly from the primary one. In the latter she was a miserable, querulous, hysterical invalid, and remembered nothing of her secondary life, which was superior, both intellectually and physically, to her primary one. In it she was gay, active and intelligent, and remembered not only all the events which had taken place in former attacks of secondary consciousness, but also those of normal life. As time went on the frequency of the secondary attacks became greater and their duration longer, till at the age of 24 they commenced to exceed the periods of normal life. From 24 to 27 she remained in the normal state. After this the secondary attacks became more and more frequent, and finally almost completely occupied her entire existence. In 1875 Félida, who was then 32 years of age, told Azam that she still suffered from attacks associated with loss of memory. These so-called "attacks," however, were simply lapses from her secondary consciousness into her original primary one. Thus, once when returning from a funeral she felt her attack, *i.e.*, her normal state, come on. She became unconscious for a few seconds, without her companions noticing it, then woke in the primary state, absolutely ignorant of the reason for which she was in a mourning carriage. Accustomed to these accidents she waited till, by skilful questions, she was able to grasp the situation, and thus none of those present knew what had happened. Later, she lost her sister-in-law after a long illness, and, during a relapse into the normal state, knew nothing about her death, and only guessed at it from the fact that she was in mourning. In the earlier periods the transition from one state to another was marked by a period of more or less prolonged unconsciousness. As time went on, this diminished and, finally, the loss of consciousness became so brief that Félida was able to disguise it. In 1887, when Azam published the account of the case, Félida was 44 years of age and her lapses into normal life had become more and more rare.—*Hypnotisme double Conscience et Altérations de la Personnalité*, par le Dr. Azam. Paris, 1887, J. B. Ballière et Fils.

In 1888 Dr. Ladame, of Geneva, communicated a somewhat analogous case to the Société Médico-Psychologique, which had been cured by suggestion.

In the cases just cited, the first attack of secondary consciousness was frequently preceded by shock, although sometimes it arose without apparent exciting cause. In subsequent ones it was usually more difficult to trace the exciting cause; generally the attacks were independent of the patient's volition, although cases are recorded by McNish and others where the state could be induced at will.

The attacks of secondary consciousness usually terminated spontaneously, and without discoverable cause. In some instances, however, the accidental reading of an account of their lost selves seems to have evoked some of the memories of the primary state and contributed to the disappearance of the secondary one.

(*b*) *Facts in support of a secondary consciousness drawn from normal waking or sleeping life.*—Here the evidence is not so clear as in the preceding section, but without the hypothesis of a secondary consciousness, it is difficult to explain phenomena such as the following:—

(1) Time appreciation in cases such as those of Savage and Hartog. Here, no ordinary physiological explanation is possible, and, while the ordinary consciousness was asleep, an intelligence of some kind must have watched the passage of time.

(2) The recollection of forgotten facts without the association of ideas connected with normal memory. Everyone, I think, must recall instances in which he has tried to remember a forgotten name, and, after having failed to recall it by every device imaginable, at last put the problem on one side in disgust and turned his attention to other things. Later, the forgotten name rises into consciousness, with a suddenness which is startling, and no association of ideas can be discovered to account for its appearance.

(3) Literary problems, which are vainly struggled with when awake, are sometimes apparently solved in sleep. Thus, on awaking, page after page is easily and satisfactorily

written, while the day before the author had been unable to find expression for his thoughts.

(4) According to Myers, works of genius, instead of being the result of an infinite capacity for taking trouble, are due to the intelligent action of a secondary consciousness. The labour is performed in a subterranean workshop, as it were, and then presented in completed form to the normal consciousness. The latter not only believes that it has done the work itself, but thinks that this has been performed instantaneously.

(c) *Hypnotic phenomena which apparently support the theory of a secondary consciousness.*—These are too numerous to be referred to in detail, and it might even be claimed that every deeply hypnotised subject shows evidence—in memory changes alone—of the existence of a secondary consciousness. In the waking state, he can recall nothing of what has passed in profound hypnosis, but when hypnotised, not only remembers the events of previous hypnoses, but also all that his ordinary memory can recall of waking life and even, in addition, much that it had forgotten. Further, he has acquired a control over his own mind and body without parallel in waking life. He can alter the rhythm of his pulse, control his secretions and excretions, and increase or arrest the activity of his special senses. He can induce anæsthesia and analgesia, and, even when all the phenomena are elicited by the suggestion of the operator who has hypnotised him, maintain consciousness and volition unimpaired. From the therapeutic side he can obtain relief from the pain of disease or injury, procure sleep at will and for as long or as short a time as he wishes. He can escape from obsessions, conquer the diseased craving for alcohol and narcotics, and get rid of numerous functional nervous disturbances. Finally, he can be taught to hypnotise himself, and from henceforth—free from all external interference—can by self-suggestion produce phenomena identical with those just described. All these phenomena cannot be evoked in every case, but something can always be effected beyond the power of the waking will.

The following is an interesting example of the spontaneous and intelligent action of the secondary consciousness in an untrained hypnotic subject. I questioned Miss A. (the subject of the time experiments above referred to) during hypnosis, as to her mental life in previous hypnoses. She replied as follows:—"When you do not speak to me and nothing occurs that interests me directly, I generally think of nothing and pass into a condition of profound restfulness. Once, however, I had an important dress to make and was puzzled how to do it. After you had hypnotised me and left me resting quietly, I planned the dress. When I awoke, I did not know I had done so and was still troubled about it. On my way home, I suddenly thought how the dress ought to be made and afterwards successfully carried out my ideas. I believed I had found the way out of the difficulty there and then in the waking state, I now know I did so some hours previously when hypnotised." When the subject was aroused, she had no recollection of what she had said and still believed she had planned the dress when awake. The origin of this feat in dressmaking—one apparently beyond the subject's normal powers—may be taken as illustrating the possible source of the higher intellectual achievements of genius.

Finally, there is evidence which shows, not only that there is a secondary consciousness which alternates with the primary one, but also that the two may act simultaneously and independently of each other. This is clearly demonstrated by the phenomenon of automatic writing.

Automatic Writing.

In choosing a subject for automatic writing two things are essential, viz.: (1) he must be a somnambule, *i.e.*, retain no memory on waking of what has passed in the hypnotic state, and (2) hypnosis must be capable of being induced and terminated instantaneously. Thus, when the subject is aroused immediately after the suggestion has been given, the problem must be solved in the waking state, although, as we shall see, not by the waking consciousness.

I have often made the following and similar experiments.

I ask a subject while awake to write down a few verses; these I take charge of and do not show him again. I then make him read aloud from some book previously unknown to him, this being chosen in order to engage his entire attention. While reading I hypnotise him suddenly, place pencil and paper near his right hand, and suggest: "On waking you will go on reading where you left off, and at the same time write down how often *b* (or any other letter selected) occurs in the verses you gave me. Wake up." He wakes, resumes reading, and at the same time writes down the answer to the problem suggested. This, almost invariably correct, is often done so rapidly that I have not had time to count the letters, even with the verses before me. I now tell the subject to stop reading, and ask him what he has written. He replies, "Nothing," and when I show him the paper, is astonished and declares he does not know what it means. I then re-hypnotise him, whereupon the lost memory returns, and he not only recalls the suggestion, but also the fact that he has carried it out.

Thus, the primary waking consciousness retains no recollection of the hypnotic suggestions. It does not know that the secondary consciousness, after the hypnotic state has been terminated, first solves the problems, and then directs the motor acts which record them. It is also unconscious of the motor acts themselves.

Gurney made many interesting experiments with healthy non-hysterical men, which illustrate the severance of the normal, or primary, from the latent, or secondary, consciousness. Of these the following are examples:—(1) The first were simple cases which involved memory, but not independent thought. Thus, Gurney showed P., one of his subjects, a planchette and made him write his name with it. P. was then hypnotised; told that it had been as dark as night in London on the previous day, and that he would record this fact in writing. On awaking he remembered nothing. His hand was then placed on the planchette—a large screen being held in front of his face, so that it was impossible for him to see the paper or the instrument—and in less than a minute he wrote, "It was a dark day in

London yesterday." (2) In the next experiments statements were impressed on the subjects, but nothing was said as to subsequently recording them. After waking, however, the writing was executed as before. (3) Gurney made more complicated experiments with another subject. During hypnosis questions were asked about his past life, or arithmetical problems suggested. He was then awakened immediately, before he had time to think of a reply, and, to engross his attention, told to count backwards from a hundred; meanwhile the planchette wrote the correct solutions of the problems. (4) Further experiments involved the reckoning of time. These, however, were not confined to the execution of an order at a given moment, but involved, in addition, other calculations made in the waking state *at a suddenly selected moment*, regarding which nothing had been previously said to the subject. For instance, during hypnosis, he was told to do something at a given date, and also that, before this time arrived, he would be required to write down the number of minutes that had passed since the suggestion was given, as well as the number that had to elapse before its fulfilment. In the interval, when his hand was placed upon the planchette, he generally wrote the answers to the problems. The results, allowing for the time occupied in writing, were remarkably accurate.

Remarks.

The experiments in groups Nos. 3 and 4 showed, according to Gurney, that the hypnotic substrata included higher physical functions than mere random spurts of memory, viz., processes of deliberate reckoning and reflection, which it would be almost impossible to conceive as having only a physiological existence. In group 4, the order itself was remembered and realised by the secondary consciousness, while the primary consciousness was wholly without knowledge of it. In Gurney's opinion, these so-called automatic writings were, in most cases at all events, intelligent and involved mentation. When a statement was made which the subject was told he was afterwards to record in writing, the performance might possibly be regarded as an exclusively automatic one, due to a "setting of the organism." Sometimes, however, the impression was made without a hint as to the future—without the faintest suggestion that it would produce any result whatever; yet, in the midst of quite irrelevant surroundings and experiences, the phenomenon appeared as soon as the opportunity of "automatic" representation arose. Here the organism could not have been specially set for the effect. Further, if we regarded the action as purely automatic, we should be compelled to concede a singular power to hypnotic impressions, viz., that of storing up energy in the brain which would work mechanically outwards along the motor nerves, as soon as the act of writing was sufficiently easy for the muscles. Moreover, memory on re-hypnotisation afforded strong evidence of mentation. Not only did the subject remember the original idea conveyed to him, and the fact that he had written something, but also the exact words he had used to convey his conception of the impression. Surely this indicated an intelligent apprehension of the words. We have seen that the memory of these so-called automatic acts could be recalled in hypnosis, but some of them, in addition, indicated the existence of a hypnotic memory superior to the normal one, as the facts recorded had occurred at an early period of the subject's life and had long been forgotten.

(II.) *Granting the existence of a secondary consciousness, how far does this explain all the phenomena we have been considering?*

The facts just cited—and these might be supplemented by many more — apparently indicate not only that a secondary consciousness exists, but also that it can act simultaneously with, and independently of, the primary one. Even, however, if we grant the existence of a secondary consciousness, this does not explain all the phenomena of time appreciation and arithmetical calculation that we have been considering.

Obviously if the intelligence of the secondary consciousness were at all comparable to that of the primary one, it would not be difficult for it to calculate the arrival of the

39th or the 123rd day from any given date. In Gurney's cases, it apparently performed this feat with ease, and the subject, when hypnotised, could recall the manner in which it had been accomplished.

Here the secondary consciousness apparently acted in just the same way as the primary one might have done under similar circumstances; having to execute an order on the 39th day from a given date, it recalled the fact from time to time and noted how many days had passed and how many had to come. Many of the experiments I have cited, notably the more complicated ones executed by Miss A., present more difficult problems, and by none of the theories already considered can these be properly solved. Bernheim's explanation, as we have seen, is in opposition to observed facts, while Gurney's objections to that of Beaunis apply with even greater force to my cases. Thus, if there is little analogy between ordinary physiological periods of time, and, for example, 39 days chosen suddenly and arbitrarily by human volition, the analogy is still less between the former and, say, 20,845 minutes.

Further, the secondary consciousness theory, while it affords a reasonable explanation of the way in which Gurney's subjects carried out their suggestions, fails to account for much that is important in the cases I have cited. The following are the principal points which demand explanation:—(1) The want of hypnotic memory as to the manner in which the suggestions were carried out. (2) The fact that the suggestions not only involved feats of arithmetical calculation and memory far beyond the subject's normal powers, but also in some cases beyond their hypnotic ones. (3) The difference in the nature of the time appreciation required in Gurney's cases and in those cited by me.

(1) *The want of hypnotic memory as to the manner in which the suggestions were carried out.*

According to Bernheim, the hypnotic subject is conscious in all stages, and all the memories of hypnotic life, which are lost on waking, can be restored by suggestion or other means. This statement is not absolutely correct. Hypnotic life, it is true, is more conscious than the normal one, and lacks the prolonged and regularly recurring periods of unconsciousness, represented in the latter by sleep. Sometimes, however, deeply hypnotised subjects receive impressions, and even perform acts, of which they are unconscious.

Thus, (*a*) where anæsthesia has been induced for surgical purposes, the subjects can recall nothing of the operations, either when awake or in subsequent hypnoses. Generally speaking, present forgetfulness does not prove past unconsciousness. When we find, however—in the instances where analgesia and hyperæsthesia have been simultaneously excited—amnesia as to certain sensations, associated with hyperæsthesia as to others, we have reasonable grounds for inferring that the sensations, which cannot be recalled, never reached consciousness. This view is further strengthened by the fact that the operations were characterised by absence of shock, persistence of analgesia after waking and unusual rapidity in the healing process.

(*b*) If a subject is told to be unconscious of everything until aroused by the operator, he will, if neither questioned nor touched, take no notice of what is said or done around him, while suggestion, in subsequent hypnoses, often fails to revive any memory of what has taken place.

(*c*) If a simple movement is suggested, of which volition does not disapprove, it may after a time become automatic, *i.e.*, after having been frequently consciously and voluntarily performed, it may be executed unconsciously, as a genuine automatic act, in response to the habitual stimulus which has excited it. Here, again, the lost memory cannot be recalled by suggestion in subsequent hypnoses.

With the exception of examples of the three classes just cited, the acts of hypnotic life are performed consciously and can be recalled by suggestion in subsequent hypnoses. Further, as the hypnotic memory is more exact and far-reaching than the normal one, the absence of memory as to some given circumstances of hypnotic life, other than those just cited, is markedly suspicious. These suspicions are deepened when the forgotten act is analogous to those invariably remembered by the hypnotised subject. Gurney's subjects easily remembered their calculations as to the days that had passed, those that had to come and the terminal time of the experiment. In some instances, when the arithmetical problems involved were simple, Miss B., in subsequent hypnosis, recalled the fact that she had calculated out the terminal time of the suggestions and set herself to carry it out at the appointed hour. This, by the way, Gurney asserted hypnotised subjects never did. When the experiments became more complicated, Miss B. ceased to do this, and then, like Miss A., was unable to revive in hypnosis the slightest trace of memory, as to the manner in which the suggestions had been carried out—they could then recall no calculations and no time watching, no foretelling of the terminal time and no recognition of it when it arrived. Yet, from what we know of hypnotic memory, it is impossible to doubt that if calculations and observations of this kind had been made by the subject, they would have been able to have remembered them when again hypnotised.

(2) *The fact that the suggestions not only involved feats of arithmetical calculation and memory beyond the subject's normal powers, but also in some cases beyond their hypnotic ones.*

Delbœuf pointed out that his subjects, in the normal state, were unable to make the necessary calculations involved in his time experiments; therefore the success of these experiments, he said, demonstrated that the subjects when hypnotised had an idea of the passage of time, and unconsciously calculated when the suggestions fell due. Experiments made in hypnosis, however, showed that the subject was quite incapable of calculating even much simpler problems than those involved, and, although this fact was recorded by Delbœuf himself, he apparently missed its significance. When Miss A. was asked to calculate in hypnosis when the suggestions fell due, she was wrong in the first nine instances, her errors frequently being extremely gross ones. Again, unless specially asked to do so, the secondary consciousness apparently made no calculations at all. The time appreciation, however, could not be carried out independently of *such* calculations, obviously the subject could not perform an act at the expiration of 40,845 minutes unless she—or some self, or consciousness, within her—knew the terminal time this represented.

Further, in Miss A.'s case the hypnotic memory was apparently incapable of retaining the complicated series of figures which were read to her. When she was questioned about them in subsequent hypnosis, but before the fulfilment of the suggestions, she always recalled that the latter had been made, but rarely correctly remembered their details—her recollection being less and less distinct in proportion to the time which had elapsed since they had been received.

(3) *The difference in the nature of the time appreciation required in Gurney's case and in those cited by me.*

There is a marked difference between the recognition of a particular day on its arrival and the last minute in such a series as 20,845. A secondary self or intelligence, which can count the days that have passed and those that have to come and refreshes its memory by doing this every night, could have no difficulty in recognising the terminal day. The varying impressions from the external world, which tell us that a new day has dawned, would be received as freely by the secondary as by the primary consciousness, and all that the former would have to do would be to associate them with the calculation it had made the night before, that the next day would be the suggested one. In my cases the problem is a widely different one. Granting that some intelligence worked out the arithmetical portion, and determined that the suggestion fell due, for example, at 3.25 p.m. a fortnight later, the determination of the arrival of 3.25 differs widely from the recognition of the dawning of a particular day. Admitting that some intelligence, equal to the primary one, tried to determine when this moment arrived, circumstances, often specially arranged, added to the difficulties of the task. In some instances, for example, Miss A. was in a darkened room for several hours before the suggestion was executed, and absolutely without any of the ordinary methods of determining the time. Even if she knew what o'clock it was when she entered the room at noon, how could she determine when it was 3.25?

The general conditions of memory, then, in reference to the experiments I have cited, apparently show that the secondary consciousness—or at all events such manifestations of it as Gurney describes—did not participate in them at all. Further, the feats in calculation and memory were beyond the power of that consciousness, while we have no evidence of the secondary consciousness carrying out time appreciations comparable to the particular cases involved. Some intelligence, however, must have made the arithmetical calculations, and, further, corrected them when they were erroneously worked out by the secondary consciousness. Something also must have remembered the complicated series of figures and the varying results of the calculations, and also, in some fashion, noticed the time as it passed and connected this with the date given as the result of the calculations involved in the suggestions. Could the problems have been worked out by a third consciousness acting independently of the primary one? The theory that a multiple, as well as a secondary, consciousness exists is not a new one, although, as far as I know, it has not yet done duty in explaining the phenomena of time appreciation. I propose now to examine some of the alleged cases of multiple consciousness, and later to see what light, if any, they throw upon the problems we have been considering.

Cases of So-called Multiple Consciousness.

Sarah L. was the first person in whom I found any evidence of so-called multiple personalities, and when she came under my notice about ten years ago I knew nothing of the literature on the subject. In the normal state she was quiet, respectful and somewhat shy, and retained this character when I hypnotised her. She was a profound somnambule; in the waking life she knew nothing of the events of hypnosis, but in hypnosis could recall all the memories of the normal state as well as the incidents of hypnotic life. In 1889, the late Mr. Bendelack Hewetson, of Leeds, operated on her for double strabismus, the only anæsthetic employed being hypnotic suggestion. Later, she sustained a severe fracture of the nose; there was a good deal of displacement and the parts were swollen and extremely painful. Profound anæsthesia was again induced by suggestion and the bones moulded into position; in each instance the occurrence of subsequent pain was entirely prevented by suggestion. Further, the patient was also cured of attacks of migraine, from which she had suffered since the age of 7, while, after fifteen months' amenorrhœa, menstruation appeared at a suggested date. The above details are cited in order to show the genuine and profound character of the hypnosis.

Before coming under my care Sarah L. had been hypnotised and exhibited by a stage performer, and, some time after the events just recorded, her mother told me that Sarah occasionally hypnotised herself, and that the condition then differed markedly from the one I induced. After some coaxing the girl consented to hypnotise herself, and went through the following performance:—First, she closed her eyes and appeared to pass into a lethargic state, then, a few minutes later, awoke with a changed expression; instead of having a shy and modest air, her eyes sparkled and she looked full of mischief. In place of addressing me as "Sir"—she had formerly been a servant of mine, and an extremely respectful one—she put her hand on my arm and said in a familiar way, "I say?" She then began to ask me impertinent questions about the persons she had seen at my house, and to criticise them in a particularly free and sarcastic fashion. The performance was so interesting and amusing that I got the patient to hypnotise herself on a good many occasions. The same phenomena always appeared; she invariably became familiar, inquisitive and sarcastic, while her highest praise for anyone she approved of was conveyed in the words, "She'll do." Other facts were noticed and reported to me by her mother. Thus, sometimes when Sarah hypnotised herself, she would remember that her mother owed her a few coppers and insist upon having them at once. If they were refused, she would take them by force; to this, however, her mother lent herself. The girl would then generally go out and buy oranges, and, on her return, eat them all herself; this selfishness was quite out of keeping with her normal character. Sometimes, when her mother asked her to do work that was distasteful to her, such as blacking the grate, she would induce self-hypnosis with profound lethargy and remain apparently deeply asleep for hours. I never taught her to hypnotise herself, nor, as far as I could learn, had this been done by anyone else. During this third stage she remembered everything that had happened in previous conditions of this kind, and also the events of the normal state and those of ordinary hypnosis, but the waking consciousness and the ordinary hypnotic one knew nothing of the events of this third state. After I had observed the condition for some time, I concluded that it was not likely to be beneficial to the patient, and suggested, during ordinary hypnosis, that she should lose the power of creating it. The suggestion was successful and the condition never reappeared.

Pierre Janet has been fortunate in finding several patients who apparently possess multiplex personalities, and has published full and interesting accounts of their cases. Amongst these that of Léonie —— is, I think, one of the most striking. This patient, aged 45, apparently possessed three distinct and well-marked personalities, viz., Léonie I.; the Léonie of normal life, a serious and sad peasant woman, calm, slow, gentle and timid. Léonie II.; Léonie in the ordinary hypnotic state, a gay, noisy, restless being, given to irony and bitter jesting, who describes her visitors in an impertinent fashion and apes their airs and graces. Léonie II. refuses to identify herself with Léonie I., and calls the latter a stupid woman. Léonie has had attacks of natural somnambulism since she was three years old, and from 16 upwards has been frequently hypnotised by various people. Now, when Léonie II. is called to the front, she knits together the events of her natural and induced hypnotic state and forms the history of her life from them; the memories of waking life are not forgotten, but these are ascribed to Léonie I.

When Léonie II. is hypnotised more deeply there appears a third personality, Léonie III., who is grave, serious, slow in speech and movement. This Léonie separates herself both from Léonie I. of waking life and the Léonie II. of the ordinary hypnotic state. The former she describes as a good, but rather stupid woman, and the latter as crazy. "Fortunately," she says, "there is nothing of me in either of them." Léonie I. knows herself alone; Léonie II. herself and Léonie I., while Léonie III. not only knows herself but also the two others. Léonie I. has only a visual consciousness; Léonie II. has both visual and auditory, while Léonie III. has a visual, auditory and tactile one. Léonie I. is embarassed and ashamed when Léonie II.'s friends, who are strangers to her, speak to her in the street. Léonie II. spontaneously writes letters, which Léonie I. finds and destroys, as she does not understand them. Afterwards Léonie II. hides her letters where she knows Léonie I. will never look for them. Léonie II. visits places where Léonie I. has never been, then disappears and pushes Léonie I. to the front, leaving her frightened by her strange surroundings.

According to Janet these three personalities, which deny and despise each other, not only existed in successive forms, but did so simultaneously. While Léonie I., for example, is apparently the only Léonie, other personalities are inside of the same woman, each of them sensible and wide awake and occupied with her own affairs.

In "An Experimental Study of Visions" (BRAIN, 1898) Dr. Morton Prince records some interesting experiments which he made with Miss X., a patient who suffered from hysterical neurasthenia. Miss X. was easily hypnotised and at first passed into the ordinary deep stage, then, when ordered to sleep more profoundly, a fresh condition developed, which differed both from that of waking life and ordinary hypnosis. According to Dr. Prince those stages formed three distinct personalities, viz.:—

X. I. The Miss X. of ordinary waking life, who is reserved, morbidly conscientious, self-contained, serious, deferential and dignified.

X. II. The Miss X. of the primary hypnotic condition, who is sad, serious, and apparently weak and suffering.

X. III. The Miss X. of the secondary or deeper hypnotic state, who is flippant and jovial, free from all physical infirmities, full of fun and reckless.

X. I. remembers the events of waking life alone and knows nothing of X. II. and X. III., while X. II. remembers all that has passed in previous primary hypnotic states, also all that X. I. can recall, and, in addition, some other events of waking life which X. I. has forgotten.

X. III. remembers all the events of the secondary or deeper hypnotic stages, as well as everything X. I. and X. II. can recall. In addition, she can describe incidents in the past life of X. I. which are lost to the memory of the latter, and can thus explain much that the waking personality is at a loss to account for. She knows all about many of the little absent-minded doings of X. I., and does not hesitate to voluntarily tell of them, although X. I. is morbidly and unnecessarily reserved about her whole life.

Dr. Prince made this tripartite personage look into a globe, which took the place of the ordinary glass ball used in crystal gazing, and describes the visions which the different personages saw. The following is one of the most interesting of these :—

X. III. was the person in action and voluntarily related the following incident, telling it with great gusto as a joke against Miss X. (X. I.), whom she talked of as "She." "'She' received a letter from a photographer yesterday. 'She' put it into her pocket where 'She' had some bank-notes. Then, as 'She' walked along, 'She' took out the money and tore it to pieces, thinking it was the letter. 'She' threw the money into the street." In response to questioning X. III. repeated the words of the photographer's note and counted mentally, with some difficulty and concentration of thought, the amount of money. X. III. said that "She" was absent-minded and thinking of something else when "She" tore up the money. Hypnosis was now terminated and the ordinary personality, X. I., appeared, who, in reply to questions, stated that she had received a letter from her photographer which she had torn up, and that she had the bank-notes in her pocket. She was asked to show them and produced the letter. This surprised her, but she thought she must have left the bank-notes at home, and could not believe she had destroyed them. The notes were undoubtedly lost, and an account of the occurrence, similar to that given by X. III., was obtained by making Miss X. (X. I.) look into the globe and suggesting that she should see what had really happened. Here, apparently, the ordinary hypnotic state, namely, X. II., was induced by indirect suggestion and fixed gazing, and the vision appeared in response to the suggestions of the operator.

Crystal gazing, the method employed by Dr. Prince, is not really necessary for the production of hypnotic visions; it simply acts by presenting a point upon which the suggested memories are concentrated, and rendered, as it were, objective. Any memory which exists in the hypnotic consciousness can be evoked by suggestion without the crystal. Under ordinary circumstances the hypnotic subject rarely visualises his memories, but when he looks into the crystal this is a direct suggestion that he should see with his eyes what has happened. I have frequently made similar experiments with hypnotic subjects, and, in place of the crystal, made them look at the top of my stethoscope, which answered equally well.

The following account is condensed from the notes kindly supplied me by Dr. Albert Wilson, of Leytonstone.

Mary W., born October, 1882, had in April, 1895, an attack of meningitis associated with influenza. During the third and fourth weeks of the illness there was high temperature, with delirium bordering on mania, and she called people snakes and did not recognise her friends. In the fifth week, during convalescence, her character changed, and she began to give those around her names which were not their own—thus, her father was Tom, her mother Mary Ann, &c. About the sixth week attacks of secondary personality appeared. The patient would suddenly turn a somersault on the bed and then assume a new character—returning suddenly to the normal, and resuming what she had been occupied with before the attack. At first the seizures lasted from ten to fifty minutes, but increased to hours, days and weeks as the time went on. The secondary self knew nothing of the primary one and *vice versâ;* further, the secondary self had apparently lost much of the knowledge the primary one had acquired. Thus, in the second state, the patient did not know what her legs and arms were and was childish in her talk. She could write her name, however, but this she did backwards, beginning at the tail of the last letter and writing quickly from right to left—not mirror writing.

After a few months the periods of normal life become shorter, and in place of one secondary stage various others showed themselves from time to time. Of these there were sixteen in all, termed by Dr. Wilson stages *a*, *b*, *c*, *d* . . . *p*. In each stage the subject remembered what had happened during previous attacks of the same stage, but knew nothing of what had occurred in any of the other stages, while the primary personality remembered events in the normal life alone, and knew nothing regarding any of the incidents which had happened in any of the numerous other states.

At the end of a year the normal condition rarely appeared, and then only as a flash—sometimes coming to the surface for five or ten minutes, sometimes only for a few seconds.

The following stages or personalities were noted, most of them being named by the patient herself:—

(*a*) The patient calls herself "Thing"; she is vacant; knows nothing of her past life and cannot stand.

(*b*) Calls herself "Old Nick" and is passionate and mischievous.

(*c*) Here there is catalepsy with deaf-mutism, but the patient writes down all she wants.

(*d*) In this stage the patient has forgotten not only the incidents of normal life, but apparently also much of the general knowledge acquired during it. In writing she spells backwards in the manner already described.

(*e*) A stage characterised by terror.

(*f*) Here the patient calls herself "Good Thing," and is docile, but usually without power in feet or hands; this stage, however, is quite distinct from (*a*).

(*g*) The patient now calls herself "Pretty dear"; is sweet and amiable, but cannot write or spell.

(*h*) Calls herself "Mamie Wud"; in this stage she recalls the events of childhood better than when awake, but is unable to remember anything about her illness.

(*i*) This stage is somewhat like (*d*), when in it the patient knows nothing and thinks she is just born.

(*k*) Here the patient calls herself "Old Persuader," and asks for a stick to strike people with if they won't do what she wishes.

(*l*) She now calls herself "Tom's darling," and is apparently a nice child.

(*m*) In this stage she asserts that she has "no name," and is violent and unkind.

(*n*) She now calls herself "The dreadful wicked thing"; throws her slippers into the fire in a temper, &c.

(*o*) In this stage she calls herself "Tommy's lamb," and is blind and idiotic.

(*p*) In December, 1896, a further stage developed, which lasted till February, 1897. The patient now kept saying "picters," and drew beautifully, even being able to do so when she was prevented from seeing the paper on which she was drawing. The original self was unable to draw. During this stage the pupils were dilated and reacted feebly to light, while the patient was apparently insensible to sound.

As time went on, the patient, when in abnormal stages, began to have some idea of what had taken place in her ordinary life; when in the latter condition, however, she still had no recollection of anything that had happened in any of the abnormal stages. In July, 1898, she passed into a condition much more closely resembling the normal one; she was still, however, childish and called herself "Critter Wood."

At the present time (Summer, 1900) five years since the commencement of her illness, she has apparently settled down in stage (*g*), but has been taught that Mary W., not "Pretty dear," is her name. She is a fine, healthy, well-developed girl, who helps in the house and is anxious to learn typewriting in order to keep herself. Her character, however, differs slightly from her original one, and she is still somewhat childish at times.

Gurney stated that he had experimentally demonstrated the existence of positive and distinct stages of memory within the conscious portion of the hypnotic trance. The subjects of these experiments were first hypnotised lightly, and something was told them which they were asked to remember. Deeper hypnosis was then induced, when the subject was asked what he had just been told; it was found that he neither remembered what had been related to him, nor even the fact that he had been told anything at all. While in this deep stage, which Gurney termed *B*, some new incident was related to the subject which he was again asked to remember. He was then recalled to the lighter stage, termed *A* by Gurney, and asked to repeat what he had been told; he had forgotten what he had heard a few minutes before in stage *B*, but repeated instead what had been told him in the earlier stage *A*, in which he now again found himself. Brought once more to *B*, he similarly remembered what he had been told in that state, while he was again completely oblivious of what had been impressed upon him in *A*. On waking he retained no memory of anything that had been told him in either stage.

Many cases, of which the following is an example, were cited by Gurney to illustrate these alterations in hypnotic memory:—

S., a young man living at Brighton, was told in state *A*, the lighter stage of hypnotic trance, that the pier head had been washed away, and in state *B*, the deeper stage of trance, that an engine boiler had burst at Brighton station and killed several people. He was then brought from stage *B* back again to *A*, when he recalled all that had been told him about the accident to the pier. Hypnosis was again deepened; stage *B* appeared, and the following conversation took place between the operator and the subject:—

Operator: "But I suppose they will soon be able to build a new one."

Had the pier been present in S.'s mind, this remark, said Gurney, would naturally have been taken to refer to it, as it had formed the subject of conversation only a few seconds before. S., however, at once replied: "Oh, there are plenty on the line"—meaning plenty of engines.

Operator: "The pile-driving takes time, though."

S.: "Pile-driving? Well, I don't know anything about engines myself."

The subject was now brought back to stage *A*, and the conversation continued:—

Operator: "If they have plenty more, it does not matter much."

S.: "Oh, they can't put it on in a day; it was a splendid place."

Operator: "Why, I am talking about the engine."

S.: "Engine! What, on the pier? I never noticed one there."

Here the subject's mind had evidently again reverted to what had been told him in stage *A*.

In the above case, as in all others of a like nature cited by Gurney, the normal self knew nothing of stages *A* and *B*, and these knew nothing of each other.

Before considering multiple personality, in reference to feats of calculation and time appreciation, I wish to examine the characteristics of the various examples of secondary and multiple personality we have been considering. The cases, which present many different phenomena, may be grouped as follows:—

Class I.—Those more or less closely associated with morbid states, and presenting phenomena which range from amnesiæ with alterations in character, to conditions similar to those presented by Félida X.

Class II.—Cases of ordinary hypnotic somnambulism, which afford evidence of a secondary personality.

Class III.—Cases of hypnotic somnambulism, presumably showing evidence of multiple personality.

Class IV.—Time appreciation, &c., like those of George Savage and Marcus Hartog.

Class V.—Instances where mental work, varying from the recollection of a forgotten name to the so-called inspirations of genius, have apparently been carried out by some consciousness other than the ordinary one, and in some condition other than hypnosis.

Class I.

At the lower end of this class Hyslop, in his article on "Double Consciousness," *British Medical Journal*, September 23, 1899, includes cases in which the patients, after a seizure of some sort, performed certain acts of which their ordinary consciousness was ignorant. These varied from purposeless automatic ones to thefts committed with more or less skill or cunning, and, apparently, were neither recalled in the normal state nor in subsequent attacks. At the other end of the group Hyslop cites Félida X., whose case, already reported, differs in many respects from those just referred to. The changes in memory, whether modifications or disturbances, are the most important phenomena in connection with double and multiple personalities, and in Class I. these may be grouped as follows:—

(*a*) Cases where purposeless automatic acts occur, regarding which there is no subsequent revival of memory in any normal or abnormal state.

(*b*) Where more or less intelligent acts are executed, which again are never subsequently recalled, either in primary or in secondary states.

(*c*) Here there are two or more conditions, each characterised by distinct chains of memory: (1) The primary or normal, in which the events of ordinary life alone are remembered, and (2) the secondary or multiple, in which the occurrences of these states are alone recalled.

(*d*) Here the primary state only possesses a memory of its own life, while the secondary has a memory of its own life, and that of the primary one also. Further, the secondary self can often recall much which the primary has forgotten.

Many of the cases also differ widely in their moral and physical aspect. Thus some of the patients, who were gentle and good in the normal state, became violent and criminal in the secondary one. Others changed in the reverse fashion both morally and physically; some, like Félida, who were ill-tempered, querulous invalids in their ordinary condition, became bright, cheerful, good-natured, and more intelligent in their secondary one.

CLASS II.—*Cases of ordinary hypnotic double personality.*

These correspond with the subdivision (*d*) just given under Class I., and the secondary self is always richer in memories than the primary one. It is also, generally speaking, healthier and more refined.

CLASS III.—*Cases of hypnotic somnambulism, presumably associated with multiplex personality.*

Here varying and important changes in memory are to be observed. In typical cases we have (*a*) a primary condition, which knows itself alone; (*b*) a secondary one, which knows itself and the primary one; and (*c*) a third, which knows itself and the other two also, and can recall, in addition, much which has been unconscious in the primary life, or that has been forgotten by the primary consciousness. Usually, the secondary self is superior to the primary one, morally, intellectually, and physically, while the third, in its turn, rises above the second. Sometimes, however, as in Dr. Prince's case, the third personality appears like an evil sprite, who rejoices at the misfortunes of the primary one.

In some cases, such as those cited by Gurney, the two hypnotic selves had each a separate chain of memory and held, as it were, no communication with each other.

In Miss A.'s case the third personality only showed itself in its results—calculations, time appreciation, &c., and I never succeeded in artificially tapping it for purposes of examination. Had I been able to do so, doubtless I should have found that it could recall the calculations, &c., which presumably it had made. It is to be noted that the secondary consciousness was incapable of performing the feats in arithmetic, &c., which the tertiary one found no difficulty in executing.

CLASS IV.—*Time Appreciations, like those of George Savage and Marcus Hartog.*

Neither of these observers can trace any memory of the process by which they arrived at their results. This, however, does not prove unconsciousness or forgetfulness, as far as some personality is concerned, it only shows that, as in Miss A.'s case, we have not discovered the way of evoking the memories. The repetition of Savage's early wakings on subsequent unnecessary occasions, apparently showed that he was capable of starting, but not of regulating, the mechanism on which these depended, while Hartog apparently possessed more control over his secondary self.

CLASS V.—*Cases of Subconscious Performance of Mental Work in Non-hypnotic Conditions.*

Here, again, it has been impossible to revive any memory as to the means by which the work has been done. Judging from the analogies of hypnotic life—we may instance particularly the dressmaking experience already referred to—it seems probable that such memories exist, and that the secondary self knows how and when it did the work, which the primary one flatters itself it has performed.

The importance of memory in relation to subconscious states is insisted on, both by William James and Myers. According to the former, the theory of "double consciousness" is only, after all, a development of what is found in Locke's famous chapter on "Identity and Diversity," namely, that personality extended no further than consciousness and that there would be two different persons in one man, if the experiences undergone by that man fell into two groups, each gathered into a distinct focus of recollection. Further, says James, "It must be admitted that, in certain persons at least, the total possible consciousnesses may be split into parts which coexist, but mutually ignore each other and share the objects of knowledge between them, and—more remarkable still—are complementary."

In Myers' opinion the formation of a secondary chain of memory is the fundamental point in hypnosis and not mere susceptibility to hypnosis. This chain of memory is essential to the grouping of the various acts which manifest the secondary consciousness. This classification excludes, and I think justly so, some of the cases cited by Hyslop.

Amnesia, even when associated with alterations in character, does not constitute double consciousness. If it did the bather who had forgotten the number of his machine and lost his temper, might be described as a case of secondary personality.

What are the exciting causes of the secondary and multiple personalities?

To this question no satisfactory answer has been given. Shock, hysteria, &c., are said to be the origin of the phenomena in Class I., but these terms explain nothing. We know little of the essential conditions associated with these morbid states, nor why they should produce a severing of the personality in some instances and not in others.

Hypnotic conditions are induced by certain well-recognised methods, but I can see no logical connection between the acts of fixed gazing, concentration of attention, suggested ideas of drowsy states, and the widely varying phenomena of hypnosis. The latter do not appear spontaneously, and some of the methods described must have been employed in every case before primary hypnosis was induced, but I cannot conceive the idea that the methods explain the phenomena.

At first, I considered cases of so-called multiple personalities—where these were hypnotic in origin—as simple subdivisions of the ordinary hypnotic state, produced artificially by suggestion. The appearance of the phenomena of appreciation and calculation of time in absolutely untrained subjects—phenomena which the secondary consciousness could not produce and of whose workings it was ignorant—has caused me to modify this view.

The time appreciation of Savage and Hartog and the so-called inspirations of genius—the results of mental work, which come suddenly, as a finished product, into the primary consciousness—are as difficult to explain, as the hypnotic cases we have just been considering.

Multiple personalities, in relation to time appreciation and calculation.

In the experiments cited, especially Miss A.'s, we noticed (1) that the ordinary hypnotic consciousness possessed no recollection of having made the calculations necessary for finding out the terminal time, and (2) could not recall any form of time-watching. Further (3), the ordinary hypnotic memory was incapable of retaining the complicated series of suggestions; it remembered they had been made, but could not recall their details. The results of the time appreciation and calculation, presumably due to a third consciousness, appeared as a sudden uprush into whatever personality—waking, sleeping, or ordinary hypnotic—happened to be present at the moment. When the ordinary hypnotic consciousness had been asked to make the necessary calculations and did so erroneously, the third personality ignored these mistakes and did its work correctly. Further, the passage of the message from the third to the second personality, seemed to make a particularly strong impression upon the latter, or to leave, for some time at all events, the door of communication open between the two. Thus the second personality, which had forgotten the details of the suggestions before these were carried out, could recall them accurately a fortnight after they had been executed.

Granting that the third consciousness or personality performed the feats in calculation and time appreciation, the question still remains: "How was it able to do it?" It matters little whether we regard the third personality as really distinct, or as an artificial division of the secondary one, we have still to solve the problems as to the nature and origin of the powers of the hypnotic self, and particularly their capacity for dealing with time appreciations and calculations, such as we have been considering.

THEORIES AS TO THE ORIGIN OF THE POWERS, OR PHENOMENA, OF THE SECONDARY AND MULTIPLE SELVES.

Delbœuf's Theory.—According to Delboeuf, the various animal functions which the human waking will is now unable to influence, but which the hypnotic self can control, were the revival of a power possessed by lower animal forms —the remote ancestors of our race. These powers had dropped out of the ordinary consciousness in the process of evolution, as their association with it had become unnecessary in the struggle for existence. Granting that a limited analogy exists between lower animal types and hypnotised subjects, as to their power of influencing certain physical conditions, it would, I think, be impossible to establish an analogy between the mental and moral capacities of the latter and those of the savage or lower animal. The arithmetical powers suddenly developed by Miss A. are not likely to have been derived from some savage ancestor, who was unable to count beyond five, or from some lower animal presumably ignorant of arithmetic. Again, the same subject spontaneously solved, in hypnosis, a difficult problem in dressmaking. The ability to correctly design a garment, in accordance with the present fashion of the day, can hardly have been derived from some woad-stained ancestor, or lower animal form.

Hyslop's Theory.—Hyslop ("Double Consciousness," *British Medical Journal*, September 23, 1899), attempts to explain the phenomena of double consciousness, by a supposed *inhibition of the amœboid movements in the pseudopodic protoplasmic prolongations of the neurospongium.* As the result of this, the connection between the nerve-cells is interrupted, and the nerve currents which, under ordinary circumstances, would pass freely from one to another, now cease to do so. These physiological phenomena, he says, have their psychical counterpart; the interruption of the nerve currents, on the physical side, being represented, on the mental one, by a breaking of the seriality of thought and a loss of the elements, which go to make up consciousness and consciousness of self. To this theory various objections might be raised:—(1) The conditions which Hyslop would explain by it—"the amnesic defects which," he says, "go so far to constitute what we call double consciousness" are just those conditions which are not characteristic of secondary consciousness. It is true that some of the cases he cites, as illustrating double consciousness, were practically characterised by amnesia alone, but these, as I pointed out, must be excluded from the category, as they lack that chain of memory which is essential to the manifestation of double consciousness. Félida X., also cited by Hyslop as an example of double consciousness, must be taken as the characteristic and fully developed type of the condition we are discussing. Here, the secondary self was not only superior physically and mentally to the primary one, but it also far surpassed it in memory. As time went on, the primary self only appeared as occasional attacks of amnesia, and thus, if it is essential to have a theory to explain amnesic defects, it is those of the primary, and not of the secondary self, which demand solution. Further, those very amnesiæ of the primary consciousness form a part of the memories of the secondary one. In Félida's case the secondary personality ultimately gained a complete ascendancy over the primary one, and, after a time, her periods of normal life—rare of occurrence and short in duration—appeared to her only as an illness, characterised by forgetfulness of events occurring in what was now, to her, her normal existence. In this secondary state, there was neither decrease of volition nor anything wanting of that complete self which forms consciousness.

Hyslop, it is true, confines himself to instances of double consciousness, associated with morbid conditions, but the phenomena presented by Félida X., notably those of memory, are closely analogous to those characteristic of the hypnotic state, and his theory, if correct, should be equally applicable to both conditions. Until recently, the mental states involved in hypnosis have been little understood; the subjects have been supposed to be automata, wanting in volition and consciousness of self. The contrary, however, is the case; volition and memory are increased in hypnosis, consciousness of self is as vivid as in the normal state, and the general intelligence is often improved. It is these phenomena which demand an explanation, not the suppositious ones, which are based on mal-observations. Starting from erroneous premises, many authorities have attempted to explain the phenomena of hypnosis by an inhibition of some form or another of mental activity, and Hyslop's theory itself is simply a very old and well-known one masquerading in a novel garb. Indeed, it was clearly stated by John Hughes Bennett in 1851.

Bennett's Physiological Theory.—According to Bennett, hypnosis was characterised by alterations in the functional activity of the nerve-tubes of the white matter of the cerebral lobes. He suggested that a certain proportion of these became paralysed through continuous monotonous stimulation, while the action of others was consequently exalted. As these tubes connect the cerebral ganglion cells, suspension of their functions was assumed to bring with it interruption of the connection between the ganglion cells.

Bennett's Psychical Theory.—From the psychical side he explained the phenomena of hypnosis by the action of predominant and unchecked ideas. These were able to obtain prominence from the fact that other ideas, which under ordinary circumstances would have controlled their development, did not arise, because the portion of the brain with which they were associated had its action temporarily suspended, *i.e.*, the connection between the ganglion cells was broken, owing to the interrupted connection between the fibres of association. Thus, he says, the remembrance of a sensation can always be called up by the brain; but under ordinary circumstances, from the exercise of judgment, comparison and other mental faculties, we know it is only a remembrance. When these faculties are exhausted, the suggested idea predominates, and the individual believes in its reality. In this manner, we attribute to the faculties of the mind, as a whole, a certain power of correcting the fallacies, which each one of them is liable to fall into, in the same way that the illusions of one sense are capable of being detected by the healthy use of the other senses. There are illusions mental and sensorial; the former caused by predominant ideas, and corrected by proper reasoning; the latter caused by perversion of one sense, and corrected by the right application of the others.

In hypnosis, then, according to this theory, a suggested idea obtained prominence and created mental and sensorial illusions, because the check action—the inhibitory power—of certain higher centres had been temporarily suspended.

Bennett's theory, before it was finally enshrined by Hyslop in charmingly simple scientific phrase, had practically served the turn of all those who regarded the hypnotic personality as a limited or degraded form of the normal one. Thus, according to Heidenhain, the phenomena of hypnotism owed their origin to the arrested activity of the ganglion cells of the cerebral cortex. Because these were inhibited, sensory impressions, which usually produced movements, after passing to the higher centres and evoking consciousness, now did so by passing directly to the motor centres. This theory was accepted by Professor McKendrick, of Glasgow, and restated by him in the last edition of the "Encyclopædia Britannica," as giving a true and scientific explanation of the phenomena of so-called animal magnetism. Many objections have been successfully raised to this theory, while the supposed facts upon which it is based have been amply demonstrated to be without foundation.

Heidenhain simply reproduces the physical side of Bennett's theory, while Bernheim, although he denies all physiological change in hypnosis, faithfully reproduces the corresponding psychical one.

Bennett's theory crops up again in Vincent's "Hypnotism." Thirty-two pages are devoted to "neurons" and "dendrons," "inaptic" and "aptic" acts and reasons for rejecting the term "reflex." Finally we arrive at the hypnotic theory, which is founded simply on an inhibition of one set of functions—with an increased capacity of action in the others—the inhibition and dynamogeny of Brown-Séquard. "The stimulus," Vincent says, "instead of being dissipated amongst an indefinite number of neuronic groups, is confined to those whose function is the pure appreciation of the stimulus; the other groups, whose function is the consideration of the reasonableness of the suggestion, and the development of the stimulus in other conscious directions, are inhibited."

Sidis, in the "Psychology of Suggestion," explains the phenomena of hypnosis in exactly the same way. "There is," he says, "a functional dissociation between the nerve cells. The association fibres that connect groups into systems, communities, clusters, constellations—contract. The fine processes of the nerve cells, the dendrons, or the termination, arborisation, or the collaterals that touch these dendrons, thus forming the elementary group—retract and cease to come into contact." He further discusses which association fibres give way first, and whether the neuraxon is contracted as a whole or whether the fibrillæ alone contract and so withdraw the terminal arborisations for minute distances. All this might be of interest if it were related in any way to the subject in dispute. The phenomena to be explained, however—increased memory, intelligence, &c.—are just the exact opposite of those which have been assumed, and theories, no matter how elaborate, nor how learned in terminology, are valueless when founded upon imaginary mental states, the existence of which is simply assumed by the operator. What does it matter whether lack of consciousness or loss of memory be produced by interruption of association fibres, arrested action of ganglionic cells of the cerebral cortex, retracted dendrons or disconnected neurons, or even by *an inhibition of the amœboid movements in the pseudopodic protoplasmic prolongations of the neurospongium*, if the problems we are dealing with are actually an increase of intelligence, consciousness, volition and memory?

Janet's Theory.—According to Pierre Janet, the secondary self is always a symptom of hysteria, while the essential fact about hysteria is its lack of synthetising power, and the consequent disintegration of the field of consciousness into mutually exclusive parts. Further, the secondary and primary consciousness added together never exceed the normally total consciousnesses of the individual.

Here the generalisation is certainly far too wide. Doubtless many cases of secondary consciousness correspond with Janet's description, others, however, present conditions which are its exact opposite. Thus, while hysteria is a prominent symptom in cases of spontaneous secondary consciousness, it is, on the other hand, not necessarily connected in any way with hypnotic form. Thousands of healthy men, absolutely devoid of any trace of hysteria, have been hypnotised, while hysteria itself, instead of favouring the induction of hypnosis, renders it more difficult.

Further, as to the relation between the severed personalities and the normal total consciousnesses, James justly points out that many instances have been noted, in which the secondary self is more highly developed than the primary one. It knows, for example, all that the ordinary self ever knew, and also much that the other had forgotten, or never known. Dr. Prince's case is a typical example of this. Here, the third personality not only knew all about her own life and that of the secondary personality, but also could recall (*a*) all that the normal personality could remember, and further (*b*) many things that the primary personality had known but forgotten, and (*c*) acts which the normal self had performed automatically, or absent-mindedly, and which had only reached normal consciousness partially, if at all; (*d*) finally, the third personality recalled events which had occurred in the delirium of fever, things of which the primary self was absolutely ignorant, and indeed had never known.

None of the theories we have been examining can be considered satisfactory. No revival of powers supposed to be possessed by lower animal forms can possibly explain the entire range of hypnotic phenomena; neither, again, can they be accounted for by an interrupted connection between the nerve cells, nor by that elastic term hysteria. Gurney's theory that the secondary consciousness calculates and watches the time, just as the primary one might do, is satisfactory for those instances in which it has been proved that this has occurred. It fails, however, when we attempt to apply it to those in which the facts were absent, and in which the feats in calculation and time appreciation were beyond the powers of the secondary self.

As the secondary self is often intellectually superior to the primary one, though we don't know why, we might be inclined to admit, although equally without reason for it, that the third self transcends the second one. As all the selves inhabit one body, and as the secondary and tertiary ones have presumably access to all the information which reaches the primary, are we to suppose that they have proved the apter scholars? It seems more than fanciful to imagine that while the schoolboy's ordinary self was learning his lessons, a second boy was peering over his shoulder, as it were, and doing the work still better. What must we say, however, to the idea of a third boy learning along with Nos. 1 and 2, and surpassing both of them?

The examples, of time appreciation, we have been considering, present problems still more difficult. As we have seen, there is a marked difference between knowing a particular day on its arrival, and recognising which is the terminal one amongst a long series of minutes. For example, suppose that a suggestion to be fulfilled in 20,840 minutes fell due at 3.15 on a certain afternoon, and that from 12.20 p.m. of the same day the subject of it remained in a room, where she was deprived of all ordinary means of determining the passage of time. Granting that the subject's third personality had calculated 3.15 as the terminal time, that she had noted the time on entering the room and calculated that 3 hours and 55 minutes had to expire before the suggestion was due, and even admitting that she was able to impart this information to her primary consciousness, and to enlist its aid in her attempt to hit upon the exact moment, viz., 3.15, the question still remains, how was this done?

According to William James, our usual time appreciations—minutes, hours and days—have to be conceived symbolically and constructed by successive mental additions. To realise an hour, we must count "now!" "now!" "now!" indefinitely. Each "now" is the feeling of a separate bit of time, and the exact sum of the bits never makes a very clear impression on our minds. We have no sense for empty time and have to subdivide the time by noticing the sensations; after we have received a certain number, our impression of the amount told off becomes quite vague, and our only way of knowing it accurately is by counting, noticing the clock, or some other symbolical conception. Our estimation of the length of time varies from many causes. A time full of interesting experiences seems short in passing, but long when looked back upon; time empty of incident is long in passing, but seems short in retrospect. Time passes quickly when we are so occupied with what is happening as not to notice the time itself. When we do nothing and feel little we grow more and more attentive to the passage of time. The length of a watched minute seems incredible, because the attention is devoted to the feeling of the time itself, such attention being capable of extremely fine subdivision.

In conclusion James says, "We are constantly conscious of a certain duration—the spacious present—varying in length from a few seconds to probably not more than a minute, and that this duration (with its content perceived as having one part earlier and the other later) is the original intuition of time. Longer times are conceived by adding, shorter ones by dividing, portions of the vaguely bounded unit, and are habitually thought by us symbolically. Kant's notion of *intuition* of objective time as an infinite necessary continuum has nothing to support it. The *cause* of the intuition, which we really have, cannot be the *duration* of our brain processes or our mental changes. That duration is rather the *object* of the intuition which, being realised at every moment of such duration, must be due to a permanently present cause. This cause—probably the simultaneous presence of brain processes of different phase—fluctuates; and, hence, a certain range of variation in the amount of the intuition and its subdivisibility accrues."

Further, "the direct *intuition* of time is limited to intervals of considerably less than a minute. Beyond its borders extends the immense region of *conceived* time, past and future, into one direction or another of which we mentally project all the events which we think of as real, and form a systematic order of them by giving to each a date."

If we accept James' explanation as to the methods by which time appreciations are carried out—and I know of no other more plausible—the time appreciations of Miss A. seem still more remarkable and inexplicable.

While I have endeavoured to show that the theories as to the origin of secondary and multiple personalities—both as to the states themselves and their phenomena—are entirely inadequate, I have no theory of my own to bring forward in substitution for these. The fresh facts I have cited, although interesting, only add to the complexity of the problems we have to solve. As William James truly says, these manifestations of the "hidden self" are immensely complex and fluctuating things, which, we have hardly begun to understand and concerning which sweeping generalisation is sure to be premature. Meanwhile, he adds, a comparative study of subconscious states is of the most urgent importance for the comprehension of our nature.

HEMIATROPHY OF THE BRAIN AND ITS RESULTS ON THE CEREBELLUM, MEDULLA, AND SPINAL CORD.

BY F. W. MOTT, M.D., F.R.S.
Pathologist to the London County Asylums,
AND
A. F. TREDGOLD, L.R.C.P.LOND., M.R.C.S.ENG.
London County Council Research Scholar.

(From the Claybury Pathological Laboratory.)

THIS paper deals with three cases of partial atrophy of one cerebral hemisphere. The lesions are different in each case, both in regard to their situation and nature; but they readily group themselves into two classes, and this may be said of the numerous other cases of porencephaly, &c., which have been previously described. These groups are:—

(1) *Cortical.*—In which the lesion is confined to the cortex or underlying white matter. (Two of the cases to be described are of this nature.)

(2) *Basal.*—In which the original lesion is situated in the structures at the base of the brain, as occurred in the remaining case.

With these two varieties are associated secondary changes in other portions of the cerebro-spinal axis, and we believe that different changes occur when the lesion is confined to the cortex, and when the basal ganglia are also affected. It is proposed to first give an account of the examination of each case, and then to endeavour to point out these differences.

CASE 1.

Primary lesion of left basal ganglia (probably optic thalamus) occurring at a very early age, and probably due to occlusion of a basal perforating artery. Atrophy of left cerebral hemisphere, including basal ganglia, of left crus, left pyramid and fillet in pons and medulla. Atrophy of right half of cerebellum with its superior peduncle. Sclerosis of left direct and right crossed pyramidal tracts in cord. Atrophy of left antero-lateral column. Diminution in number of anterior horn cells in cervical and lumbar regions, affecting the lateral and postero-external groups. Clinically—epileptiform fits from infancy. Right hemiplegia with increased reflexes. Progressive dementia. Death at the age of 30 *years.*

Clinical History.

J. E., male, died in Claybury Asylum at 30 years of age of acute phthisis. Since infancy he had been subject to fits, and mentally was rather dull and stupid. At the age of 26 he became subject to attacks of maniacal excitement, so that he had to be sent to the asylum. He was then found to have right hemiplegia with increased reflexes (considered to have dated from infancy). He had frequent fits of an epileptiform type whilst under observation, and gradually became more and more demented until his death.

Post-mortem Examination.

The bones of the right hand, arm and leg are obviously smaller than the left, and the muscles are much atrophied.

The *Skull* shows no change externally, but on examining it from the inside the whole of the left half is found to be very much thicker; this is most marked in the frontal and parietal regions. Thus the thickness of the bone over the left frontal lobe is 20mm., as compared with 11mm. of the opposite side. Over the left parietal and central regions it is 12mm. as compared with but 5mm. of the opposite side. The base of the skull in the anterior and middle fossæ is also thicker on the left side. In the occipital region there is comparatively little difference between the two sides, and this is in correspondence with the fact that in this region there is but little atrophy of the brain substance. This overgrowth of bone is undoubtedly secondary to, and corresponds with, the atrophy undergone by the brain.

The *Membranes.*—Beyond some slight thickening of the pia over the wasted hemisphere, these show no change of note. There is a considerable quantity of cerebro-spinal fluid present at the base of the brain, but no abnormality of any of the vessels could be discovered.

Brain.—There is a notable difference between the size of the two hemispheres. The weight of the left is but 155 grams, whilst that of the right is 575 grams. This latter weight may be taken as normal, and as no microscopical change could be discovered on examining the right hemisphere, it may be dismissed from further consideration. On a further examination of the left hemisphere, it is found that the diminution in weight is due to a marked atrophy of the white and gray matters, the ventricle being hugely dilated in all its parts. The basal ganglia, and especially the optic thalamus, are also quite insignificant as compared with the opposite side. It is noticed that as well as the convolutions being so extremely wasted, they are simpler in nature than on the opposite side. All parts of the hemisphere are not equally affected, however; the greatest amount of atrophy exists in the central and parietal regions, next in the frontal, and least of all in the occipital. This fact is shown not only by the appearance, but also by a comparison of the weights of the different regions. There is no difference in size between the optic tracts nor the olfactory lobes of the two sides. The corpus callosum is much thinner than normal.

Portions of the cortex were removed from the frontal, central, and occipital regions, and after staining by different methods were examined microscopically with the following results:—

Frontal and central regions.—It is here that the greatest change is found. The outermost layer of cells and the layer of small pyramids are fairly normal; the large pyramids, however, are very deficient, indeed, they are practically absent, and the cells below these are also much diminished in number. With regard to fibres, there is an almost complete absence of those of the projection system, and there are also very few of either the superficial tangential fibres or of those composing the line of Baillarger. The medullary centre consists chiefly of bundles of the longer association fibres, and generally it is found that this system is least of all affected, the tangential system to a slightly greater extent, and the projection fibres most of all. The great diminution of the large pyramids and their axons is evidently a secondary change resulting from the basal lesion, the fibres being probably originally affected in the internal capsule. It is thus of the nature of a Gudden atrophy. As will be presently seen in the examination of the cord, the distal portion of the efferent tract is also greatly affected (fig. 2).

Occipital region.—The cortex of this region has undergone very little change, the difference between this and other parts being very striking. All the layers of cells can be made out, and the tangential fibres and line of Gennari are well seen. It may be here stated that the patient had no affection of sight, and that the posterior portion of the thalamus and the optic commissure and tracts appeared normal (fig. 1).

The *Basal ganglia* are much smaller than on the opposite side; the greatest difference is in the anterior two-thirds of the thalamus, where the number of cells is much diminished. The internal capsule also contains very few medullated fibres.

Pons.—There is marked atrophy of the pyramidal fibres and also of the middle fillet on the left side.

The *Medulla* is also markedly asymmetrical, chiefly due to the small size of the pyramid and interolivary fillet of the left as compared with the opposite side. In the lower portion of the medulla there is also a slight sclerosis dorso-lateral to the left olive (in the region occupied by the antero-lateral column). There seems also to be some slight diminution of the left external and right internal arcuate fibres.

No differences can be made out between the posterior column nuclei of the two sides, nor between the restiform bodies, the olives, nor the posterior longitudinal bundles, all these appearing to be quite normal.

Owing to the method which had been used for hardening the tissue, an examination of Deiter's nucleus by means of Nissl's method could not be made; but we could not discover any appreciable change between the two sides in carmine-stained sections. The changes in the pyramid and fillet do not appear to be of the kind one finds in secondary degeneration with resulting sclerosis; they consist of an actual diminution in the number of fibres, with slight interstitial overgrowth, the fillet being but half the size of the opposite one. The microscopical appearances are more like those found in the arrested development of a tract than due to degeneration occurring in a tract already fully formed. It has been seen that the lesion probably occurred before the myelination of the efferent system, and it is easy to see how a lesion at the base of the brain would involve these motor fibres.

The reason why the fillet should be so much atrophied is not at first sight so apparent. It may be thought to be due to an atrophy of fibres having an ascending direction; there is, however, no change in the posterior column nuclei. It has been seen that in the lower part of the medulla there is slight sclerosis in that

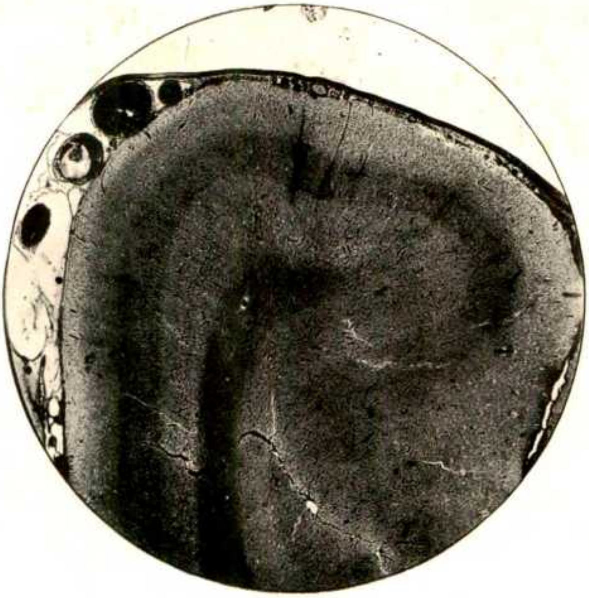

FIG. 1.

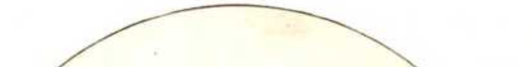

FIG. 2.

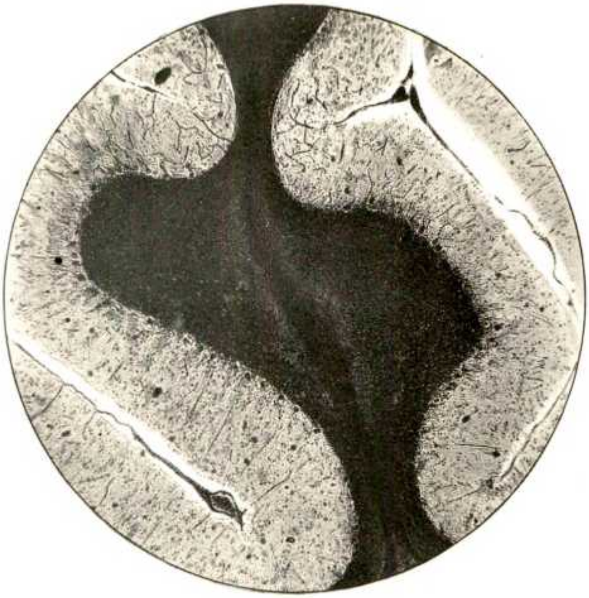

FIG. 3.

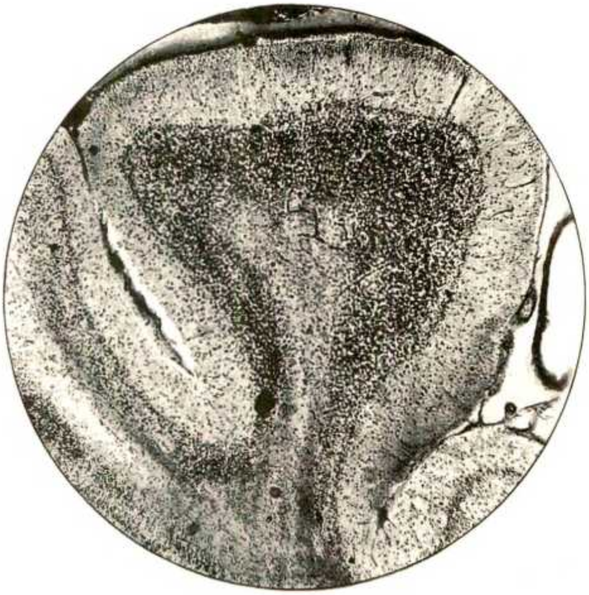

FIG. 4.

portion occupied by Gowers' tract, and it will be shown presently that there is very extensive atrophy in the antero-lateral column of the cord on the same side. Although some fibres from Gowers' tract undoubtedly ascend through the region of the fillet, these fibres are comparatively few in number, and would not account for a reduction of the fillet to half its normal size. Indeed, as will be presently seen, it is likely that the atrophy of the antero-lateral column of the cord is not due to Gowers' tract at all.

The more probable explanation of the wasting of the fillet is that it is the result of atrophy of *descending* fibres, probably having their origin in the thalamic region. There is strong evidence that there are descending fibres passing through the middle fillet of the pons and the interolivary fillet of the medulla. It will, perhaps, be better to return to this subject after the condition of the cord has been described.

Cerebellum.—Weight of left half 70 grams, of right half 55 grams. Atrophy is found in the right half only (the side opposite the cerebral lesion), and on this side it is confined to the following situations:—(1) The lobus culminis, which is affected throughout its entire extent; (2) the biventral lobule, the posterior half only of which is atrophied. The dentate nucleus is also much smaller, and contains fewer cells, although what are present appear to be normal. The superior peduncle on this side is also only a quarter the thickness of the opposite one. There is no change in the vermis nor any other part of the cerebellum.

With regard to the particular structures affected by this atrophy, there are a few points of great interest:—(1) In the atrophied region there is an entire absence of the cells of Purkinje; (2) it can be readily made out (owing to the selective nature of the changes) that the granule layer is divisible into two strata of cells.

Immediately beneath the layer of Purkinje's cells there is a layer of round cells, two or three deep, which are distinctly larger than those making up the bulk of the granules. This outer layer persists unchanged in the atrophic lobules. Normally, the deeper granules, which may be called the granules proper, are much more numerous and are smaller than these cells; indeed, they are so numerous that it is difficult to distinguish the outer layer in the normal cerebellum as it is overlaid by the granules. In this case, however, the true granules are profoundly diminished, in some places almost absent, and thus the more superficial layer (remaining unaffected) comes readily into view. The molecular zone is also thinner in the affected region, and contains fewer cells. It would further appear that whilst the atrophy especially affects these two cell groups (Purkinje's and the true granules) Purkinje's are the first to suffer, as several of the leaflets show an intermediate stage, in which but two or three of these cells are present, whilst the number of granules is still considerable (figs. 3, 4, 5).

With regard to the fibres it is at once seen that there is a great diminution. This diminution is almost entirely confined to the *large* fibres of the medullary rays, which are presumably connected with Purkinje's cells. In the absence of these fibres it is seen that the medullary substance and the region of the granules are occupied by a network of fine interlacing fibres, which would seem to belong to an association system. Further, bundles of fibres can seen passing in the medullary centre between adjacent folia, and fibres having a tangential course can be seen in the deeper parts of the molecular layer, and in the region occupied by these large granules. In view of these facts the inference is that this layer of large granules, which are the only cells remaining unchanged, are those which are chiefly in relation with an inter-cerebellar association system (figs. 6, 7).

Golgi drew attention to cells of a large kind lying in the zone of granules, and he described them as having protoplasmic processes ending in this and in the molecular zone, and with an axis-cylinder process penetrating into the granule layer and there forming an inextricable network. Cajal (quoted by van Gehuchten) and van Gehuchten himself (6), also consider these cells and their processes as an association system.

The cerebellar atrophy in this case is owing to the connection of the cerebellum with the opposite basal ganglia by means of fibres passing through the superior peduncle. This connection is now well established by numerous observations, and probably takes place by the conjunction of several neuronic systems. There are two views as to the direction of these fibres; some authorities agreeing with Mabaim (12) that they have their origin in the red nucleus, and are thus cerebello-petal; whilst Cajal (4) and others think that they arise from cells situated in the cerebellum, and are thus cerebello-fugal. The bulk of the evidence seems to show that whilst fibres may pass through the superior peduncle in both directions, the majority have their origin in cells situated in the cerebellum, as after cerebral lesions the change observed in the superior peduncle is rather one of atrophy than of secondary degeneration. It is unfortunate that

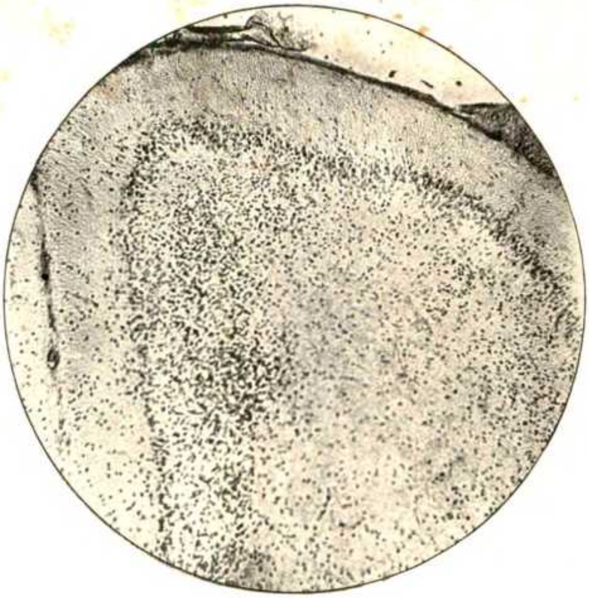

FIG. 5.

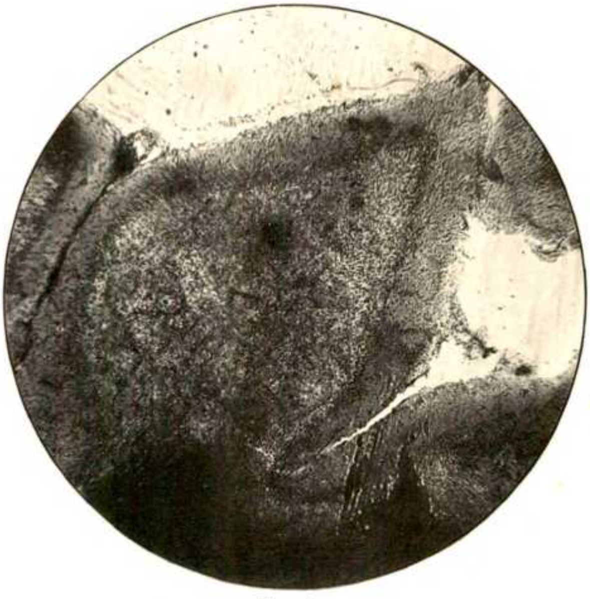

FIG. 6.

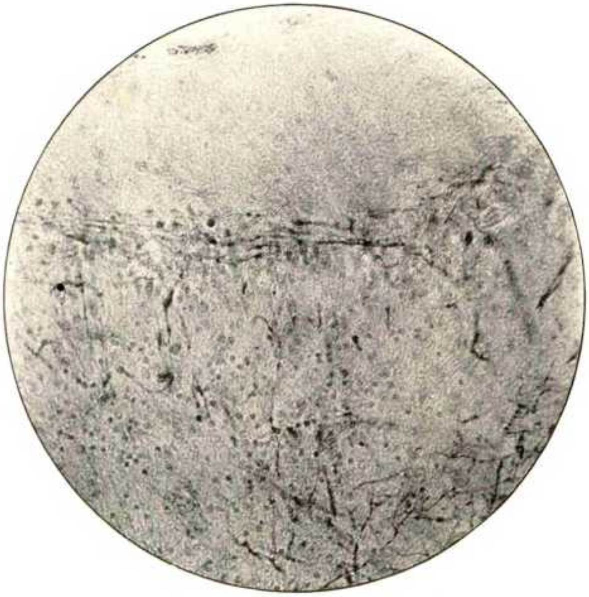

FIG. 7.

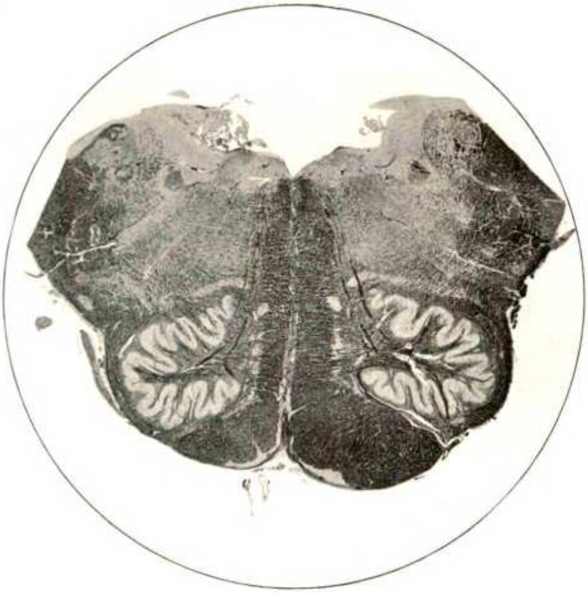

FIG. 8.

in this case the brain had been so cut that the red nucleus could not be examined. Opinions are also very much divided as to the actual origin of such cells within the cerebellum. Held (8) thinks that the larger number of such arise from the dentate nucleus. Menzel and Dejerine agree with him, finding that a lesion which involves the cortex and adjacent white matter only, does not lead to any marked change in the superior peduncle or red nucleus. On the other hand Marchi (18), Mingazzini (13) and Cajal (4) state that there *is* considerable degeneration in the fibres of the superior peduncle after extirpation of the cerebellar cortex; indeed, Cajal has shown (in the mouse) that the axones of Purkinje's cells go directly into the superior peduncle, and von Monakow (15) has recorded a case of atrophy of the right cerebrum and left cerebellum and its superior peduncle, with no change in the dentate nucleus.

The very considerable atrophy of the dentate nucleus in this case shows that fibres certainly pass between it and the opposite basal ganglia. The atrophy of the cerebellar cortex may be secondary to that of the dentate nucleus, or may be due to the involvement of other fibres passing directly to the basal ganglia without the intervention of the dentate nucleus.

Spinal cord.—This is obviously asymmetrical, the left half of the cord being much smaller than the right. The difference between the two sides gradually diminishes from above downwards. It is exceedingly well marked in all parts of the cervical region, and slightly less so in the dorsal; it can, however, be definitely made out even as far as the fourth lumbar segment. Below that level there is practically no difference between the two halves. There are two factors which bring about this asymmetry: (1) In the left and smaller half of the cord there is a well-marked atrophy at the periphery of the cord in the situation of the antero-lateral tract. The area of the crossed pyradimal tract on this side also appears to be smaller than usual, and certainly smaller than the corresponding area of the opposite side. (2) The anterior column on the right side is much larger than normal. In the photographs this is very apparent, it being readily seen that the anterior column to the right of the median fissure is almost double the size of that to the left in the cervical and dorsal regions. This inequality appears to be chiefly due, however, to an excessive size of the right, the left being only slightly less than normal. This fact, taken in conjunction with the smaller size of the left crossed pyramid, indicates that there has been an unequal crossing of the pyramidal tracts. That is to say, that as a result of the lesion at the base of the brain interfering with the efferent fibres of one side, there is interstitial sclerosis of the right crossed and left direct pyramidal tract. And that of the healthy efferent tract coming from the *right* cerebral hemisphere a great many fibres do not undergo decussation in the medulla, but are continued down the cord on the same side, partly in the lateral column, but mainly in the anterior column, where they form an unusually large direct tract. There is also slight sclerosis of a portion of the crossed pyramidal tract on the same side as the cerebral lesion. This is well seen in the photographs and is undoubtedly due to the involvement of homolateral fibres.

It has been said that there is considerable atrophy of the left antero-lateral column. This is most marked at the periphery, and causes a very evident indentation of the cord as low down as the first lumbar segment. It is in the situation of the descending cerebellar path, but we do not think it is due to involvement of that path, because the homolateral cerebellar hemisphere and the vermis are perfectly normal, nor could any change be made out in Deiter's nuclei. The condition of the cerebellum also negatives the idea that the atrophy may represent the ascending tract of Gowers, as most of these fibres go to the vermis (17). The view we take, and which seems to best fit in with the case, is that this atrophy is in a *descending* path having its origin in the thalamic region. It is probable that in the medulla these fibres pass downwards through the fillet, and it has been seen there is marked diminution in the number of fibres in this region.

Hoche (10) has recently described two cases in which he found the fillet fibres degenerated in a descending direction, such fibres going to the cranial nerve nuclei, and he further states that such descending fibres may readily be distinguished in the new-born child on account of their late myelination. Flechsig and von Bechterew have also shown that a certain number of fibres in the region of the fillet become medullated at a much later date than do the bulk of the fillet fibres. In this connection it is of great interest to note that a descending (probably) tract has been seen passing between the lower part of the medulla and the upper dorsal cord by several observers. Its situation in the cord is in the most peripheral part of the antero-lateral column. Meyer (16) described degeneration in such a bundle in a case of pontine hæmorrhage. Helweg (9) described it under the name of "Dreikantenbahn," and von Bechterew has also described a tract which seems to be identical in position. Von Bechterew (2) calls it the "Olivenstrang." He seems to think that it is an ascend-

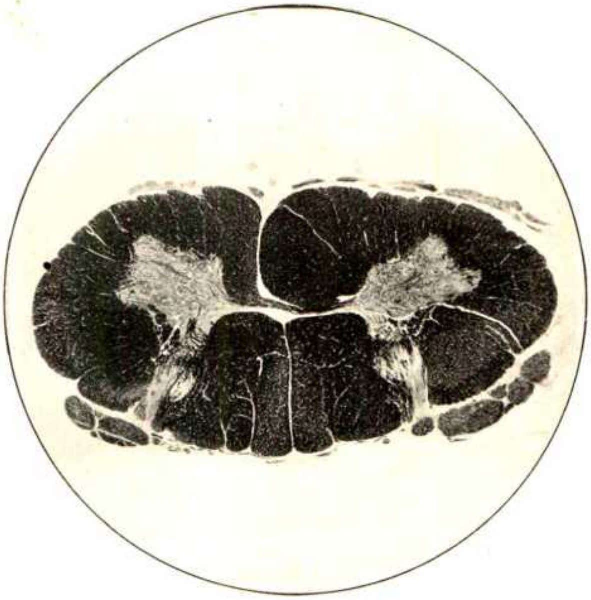

FIG. 9.

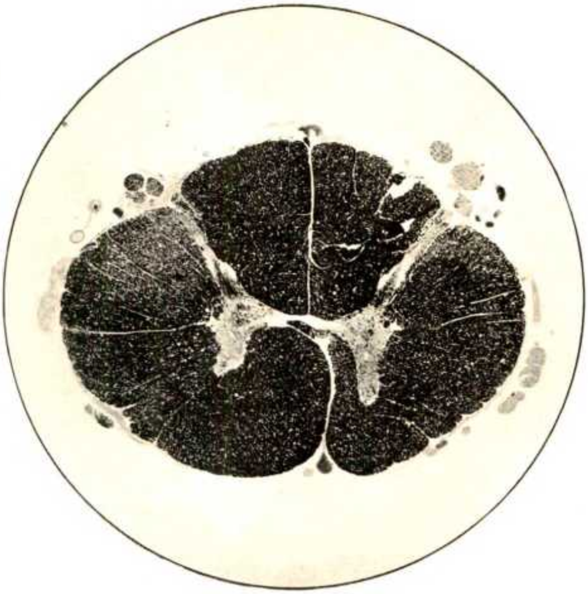

FIG. 10.

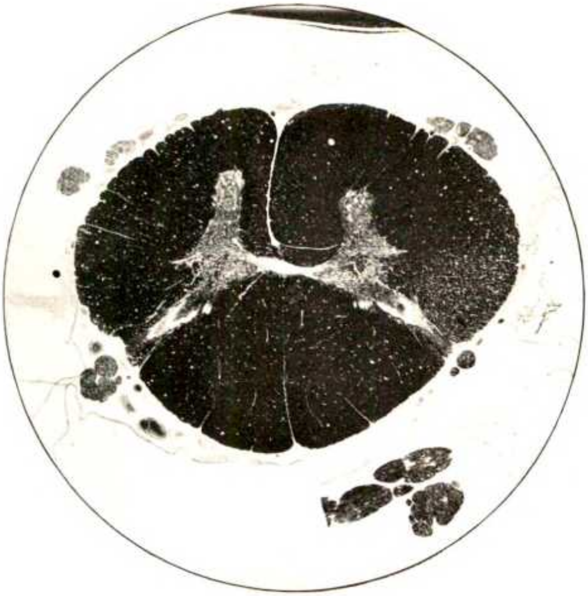

FIG. 11.

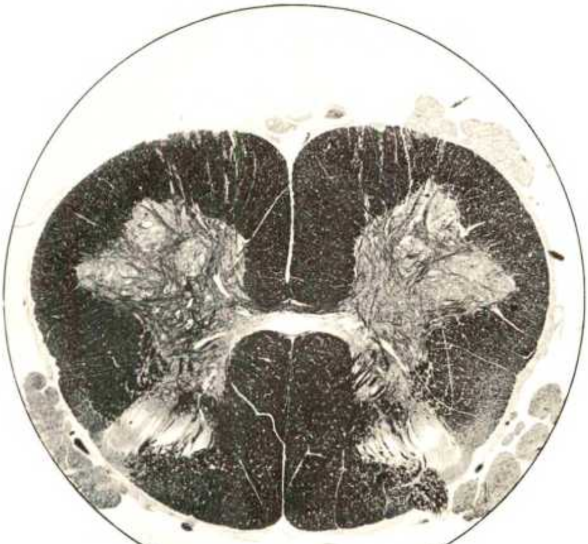

FIG. 12.

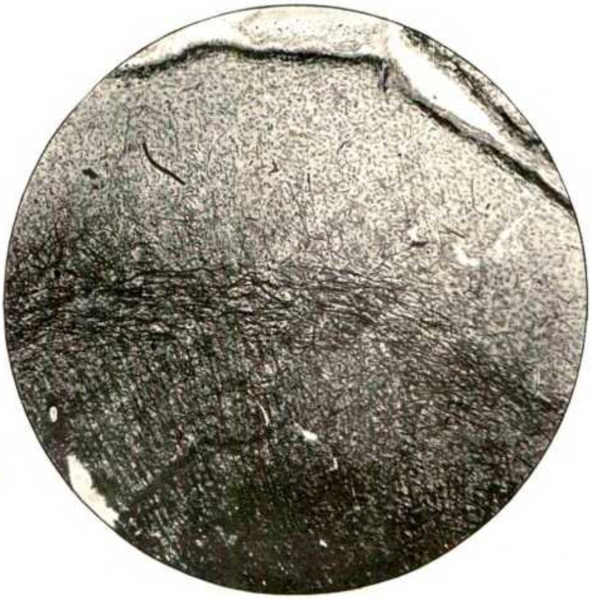

FIG. 13.

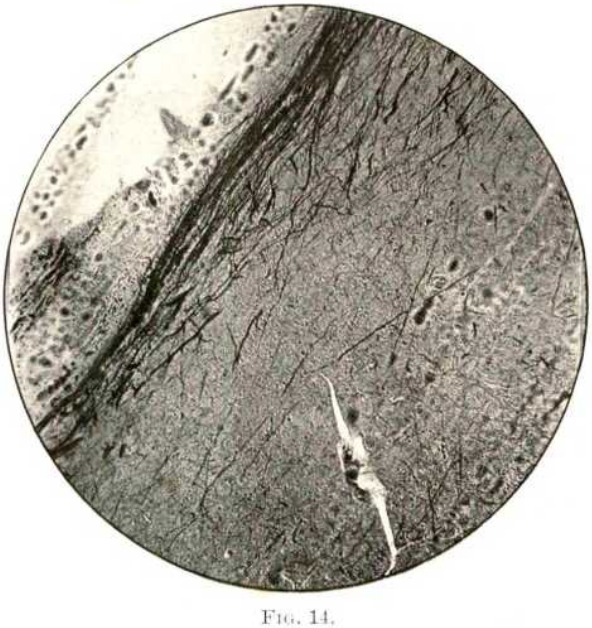

FIG. 14.

ing tract which enters into the olivary nucleus, as he has not been able to trace it above that point; he admits though that there is no proof that its fibres end there. Barker (1), who gives a very good account of this tract, has himself observed it. He is inclined to look upon it as a descending tract, and to consider that the fact that it may be degenerated whilst the olive is quite normal is against the view that it arises in that nucleus. He suggests that the fibres may come from higher parts of the nervous system, possibly being so scattered above the level of the olive that they are not readily distinguished.

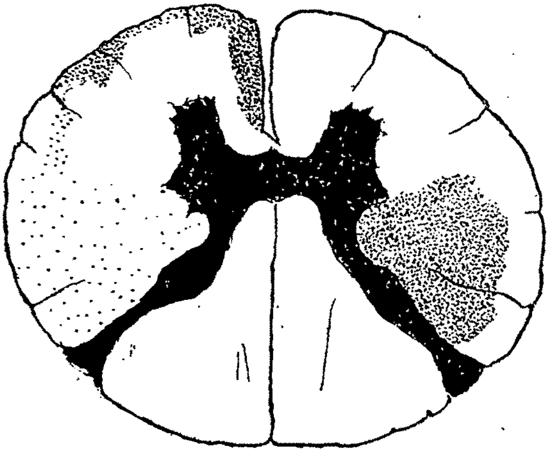

FIG. 15.

Spinal Cord.—Section at level of first cervical segment from a case of thrombosis of the left middle cerebral artery. Marchi stain. In addition to the degeneration in the direct and crossed pyramidal tracts, there is also degeneration in the antero-lateral column at the periphery of the cord on the *same* side as the cerebral lesion, also scattered degeneration (homolateral fibres) in the lateral pyramidal tract of the same side.

In this place we wish to refer to another case which we have recently examined.

Patient was affected rather suddenly with right hemiplegia. He was admitted into hospital, but died within three weeks of the onset of the first symptoms.

At the autopsy the left middle cerebral artery was found thrombosed at its commencement. No change was discovered in any of the other vessels. The greater part of the spinal cord was used for a chemical estimation, but the upper cervical region was put into Marchi's fluid and examined microscopically. In addition to the ordinary degeneration in the corresponding direct and crossed pyramidal tracts, these sections show well-marked recent degeneration of a bundle of fibres at the periphery of the cord in the antero-lateral column of the same side as the cerebral lesion; there is also degeneration of a few fibres passing dorsalwards from this towards the lateral pyramidal tract, but in this case the degenerated fibres are a little distance from the periphery of the cord. There is also scattered degeneration throughout the lateral column of the same side, doubtless due to homolateral fibres. The extent and position of the degenerated fibres are well shown in fig. 15, which is a drawing made by the Edinger apparatus, the finer details being filled in under the microscope.

In this case the degeneration in the antero-lateral column is identical in position with the change in Case 1. No other lesion than that of the middle cerebral artery could be discovered, it therefore seems fair to consider that the degenerated fibres in the antero-lateral column have their origin from cells within the area of distribution of this vessel. So that hitherto, although several observers have noticed the existence of such a tract in the antero-lateral column of the cord in the cervical region, its upward continuation above the olive and downward continuation below the cervical portion of the cord have not been shown.

We are inclined to think that the atrophy of the antero-lateral column in this case is due to the involvement of this tract; that its probable origin is in the optic thalamus; that it passes through the middle fillet in the pons and the interolivary lemniscus in the medulla to reach the peripheral part of the antero-lateral column of the cord, in which it descends as far as the lumbar region.

It has been conjectured that a descending thalamo-spinal path exists in man, although no direct proof has so far been afforded. It is well known, however, that in several of the lower animals with but little cortico-spinal connection there is a very well developed thalamo-spinal tract. We know that in man a very large number of the sensory fibres end in this region. Most of the ascending fibres of the fillet (coming by means of the posterior column nuclei from the columns of Goll and Burdach) end in the thalamus; the fillet also receives fibres from the antero-lateral ascending tract. Thus the thalamus is a large receiving station on the afferent tract, and by means of these efferent fibres just described, it becomes a large and important ganglionic station midway between the lower spinal reflexes and the higher cortical volitional centres, and probably functionating in those multitudinous semi-automatic movements which do not rise into consciousness.

Further support of this view of the importance of the thalamic region as a ganglionic station is afforded by the well known case of Goltz's dog. In this animal both cerebral hemispheres were removed, but the co-ordination of the most complicated automatic movements remained.

It may here be mentioned that we have examined the cells of the optic thalamus of a new born child by means of Nissl's method, and we find that whilst there are several distinct varieties a large number of them are evidently motor. Such cells are intermediate in size, shape, and period of development, between the motor cells of the anterior horns and the large pyramidal cells of the motor cortex.

So far no efferent tract passing directly between the cerebellum and the spinal cord has been satisfactorily demonstrated, and the researches of Ferrier and Turner (5) and Risien Russell (21) do not support Marchi's views as to the existence of such direct connection. There is certainly no evidence in this case to support the view of any such connection, unless the atrophy of the *opposite* antero-lateral column of the cord can be considered to be due to cerebellar fibres.

In view of these findings we suggest the possibility of cerebellar fibres to the cord passing by way of the basal ganglia (possibly the optic thalamus).

Ganglion cells.—In the cervical and upper dorsal regions it is evident to the naked eye that the right anterior horn has a shrunken appearance and is smaller than the left. On examining Nissl-stained sections, important changes in the ganglion cells are found. Above the fifth cervical segment there is practically no difference between the two sides; but at this level there are undoubtedly fewer cells present on the right side, and the diminution is almost entirely confined to the cells in the lateral and postero-external groups. At the eighth cervical and first dorsal segments there are identical changes affecting the same cell groups. The mesial anterior group of cells appears to be quite normal and equal on the two sides. In the upper part of the second dorsal segment similar changes are found in the right lateral group; but at this level there is unquestionably a diminution in the cells of the mesial-anterior group of the *left* side. A series of Nissl-stained sections were examined to ascertain the condition of the cells, it being quite impossible to make any reliable observations upon diminution of cells from the examination of only a few sections. To give an idea of the extent of the change we may say that in sections through the eighth cervical and first dorsal segments the number of cells in the right lateral and posterior groups was but half those in the same groups of the opposite side. In the dorsal region sections were examined from the fifth, ninth, tenth and twelfth segments. At none of these levels are there any differences between the anterior horn cells of the two sides.

The limitation of the changes to these segments is in accord with the observations of Ferrier and Yeo, Risien Russell, Allen Starr and others, who find that the muscles of the arm, forearm, and hand are enervated from the fifth cervical to the first dorsal segments inclusive. This case also shows that it is chiefly the lateral and postero-external groups of cells in these regions from which the nerves are derived, and is in accord on this point with our findings in cases of amyotrophic lateral sclerosis in which the same cell groups are those chiefly affected. In this respect the view of von Lenhossék (11) is worthy of note. He considers that the mesial-anterior group of cells are not motor but commissural in function, sending their axones through the anterior commissure to the opposite side of the cord. It is believed by Kaiser and others, however, that this group of cells supplies the muscles of the back, but from this case they certainly appear to have but slight connection with the cortex.

In the tenth and twelfth dorsal segments there is a slight diminution in the number of cells composing the right Clarke's column, and a similar change is also seen at the level of the first lumbar segment. In the lumbar and sacral regions there is again marked diminution in the motor cells of the right anterior horns, and here, too, the changes are chiefly confined to the lateral and posterior groups of cells, the mesial-anterior group showing no change. The changes here described are also seen very well in carmine-stained sections; they consist in an actual diminution of ganglion cells in certain groups, and although in the affected group some of the remaining cells are atrophied, the change is principally a quantitative and not a qualitative one.

Von Monakow (15) believes that the fibres of the pyramidal tract are not in immediate contact with the lower motor neurones, but that there is another neuronic system interposed. Schäfer (22) holds the same opinion. He finds that after lesion of this tract no degenerated fibres can be traced directly into the anterior horns, or into any part of the gray matter other than the base of the posterior horn and Clarke's column.

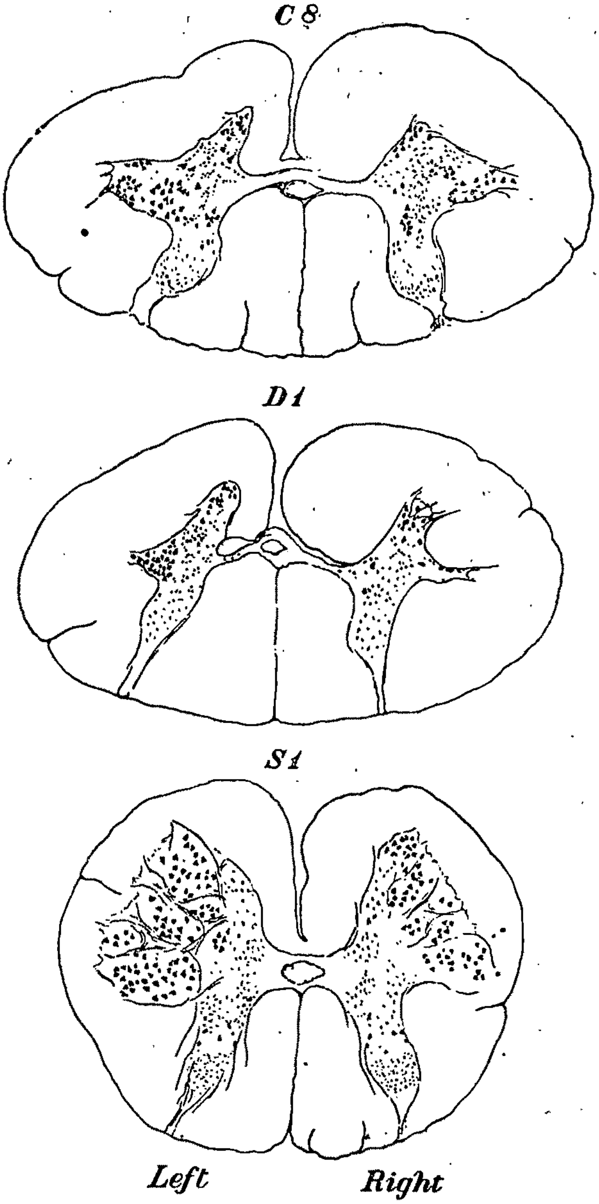

FIG. 16.

Spinal Cord.—Three drawings, by means of the Edinger apparatus, of Nissl-stained sections from case 1, showing the diminution in the number of cells in the cervical and lumbar regions, almost entirely confined to the lateral and postero-external groups.

It may be that another neurone is interposed between the pyramidal tract and the anterior horn cells; but it does not appear from this case that such junction is by means of Clarke's column, and Rothman (20) denies that the fibres of the pyramidal tract terminate in that column.

In sections through the cervical and lumbar enlargements stained by the Weigert-Pal method, there is seen to be not only a diminution in cells in the anterior horns, but also a far less plentiful network of fibres than in the normal cord, especially is this so in the centre of the horn. This rather suggests that the fibres of the pyramidal tract may here break up into a fine arborisation, and so come into immediate connection with the motor cells.

Case 2.

Atrophy of left hemisphere, involving the cortex only around the central convolutions. Basal ganglia not affected. Atrophy of corresponding efferent tract in pons, medulla and cord. No change in fillet or cerebellum. Well marked tangential, super, and inter-radial fibres. Numerical diminution of anterior horn cells in cervical and lumbar regions. Clinically—right hemiplegia from birth with (?) epileptic fits. Exaggerated knee-jerks. No dementia. Death at the age of 33 *years.*

Clinical History.

J. H. has had right hemiplegia from a very early age (probably from birth). He has also been subject to fits (? epileptic) since he was a fortnight old, but he was apparently able to partially earn his living until 28 years of age. At this age, owing to the severity and frequency of his fits, and his impulsive, violent, and unreliable mental condition, he had to be sent to an asylum. Whilst here he had frequent fits, but was able to do a fair amount of useful work in between them. At the time of his death (aged 33 years) he showed comparatively little mental degradation. We saw him a short time before his death, and his condition was then as follows:—There was paresis of the right hand and arm, the finer movements of the fingers being especially affected (opposition, abduction and adduction). This hand was blue and cold, and the muscles of the thenar and hypothenar eminences and the interossei were decidedly less developed than on the opposite side. Occasional athetoid movements were observed to take place in this hand. There was also paresis of the right foot, the finer movements here being most affected, and the muscles of the right calf were much less developed than those of the left. There was no paralysis of any muscles supplied by cranial nerves. The knee-jerks were exaggerated but equal on the two sides. No ankle clonus. Plantar, cremaster and abdominal reflexes were normal. The pupils were equal and reacted to light and accommodation. Cutaneous sensation appeared to be normal all over the body.

Post-mortem Examination.

The right hand and arm and the right leg are shorter and smaller than those of the left side.

The *Skull* is asymmetrical as seen from the outside, the left parietal eminence being decidedly less prominent than the right, and the skull being somewhat flattened in this region. There is, however, no difference in the thickness of the bone on the two sides, neither of the vertex nor the base.

Membranes.—The dura mater is normal. The piâ-arachnoid is opaque and thickened and of greatly increased vascularity over a considerable area on the external surface of the left hemisphere. This area comprises the following convolutions : The whole of the ascending frontal and ascending parietal, and the posterior portion of the superior frontal, the convolutions above and in front of the inter-parietal sulcus as far back as the parieto-occipital fissure. It is thus somewhat wedge-shaped in appearance, with the base of the wedge at the great longitudinal fissure and the apex at the anterior part of the sylvian fissure. Over this area the piâ is closely adherent and cannot be removed without causing decortication. In the other parts of the brain it is perfectly natural in appearance.

Brain.—The left hemisphere weighs 105 grams less than the right. It is shorter and smaller as a whole, but there are no cyst-like depressions and no dilatation of the ventricles. The main sulci are somewhat distorted in their arrangement and position, but with a little difficulty they can all be traced. The right hemisphere is perfectly normal in every way. The basal ganglia are unaffected and equal on the two sides. There is no change in the corpus callosum, in the olfactory bulbs, nor in the optic commissure or tracts. Portions of the cortex from several regions of the brain were examined microscopically. All those situated outside the area above described were quite normal. Within this area sections have the following appearance:—At frequent intervals there are foci in which the nerve-cells are considerably diminished in number and much jumbled up in arrangement. In these situations there are no definite Meynert's columns or even readily distinguishable layers. There is also a considerable increase of neuroglia cells and of leucocytes, and the vessels are much distended. The portions intervening between these areas approach much more nearly to the normal, but even in these there is a deficiency of large nerve-cells. Throughout the whole of the motor region affected there are comparatively few of the larger pyramids and of Betz's cells. The fibres of the projection system are also much diminished, but the tangential and interradial fibres are present in abundance (figs. 13, 14). A section from an exactly corresponding region of the opposite healthy hemisphere shows large numbers of Betz's cells, in fact, they are present to almost greater extent than we have ever observed before, thereby suggesting that a compensatory increase has taken place.

In the *Crura* the left pes is very much smaller than the right; but the red nucleus is unaffected.

In the *Pons* the left half is much smaller than the right, and there is great diminution in the longitudinal efferent fibres. There is no change in the fillet.

The *Medulla* is also much smaller on the left side, owing to great diminution in the size of the pyramid. This contains fewer nerve fibres and there is some interstitial sclerosis. The olives, the interolivary fillet, and other portions of the medulla show no change.

The *Cerebellum* is quite healthy, and the two halves weigh exactly the same.

The *Spinal cord* is asymmetrical, owing to a diminution in the number of fibres of the left direct and the right crossed pyramidal tracts. In these tracts there is slight interstitial sclerosis, but the fibres in the sclerosed tracts do not appear to be smaller than those on the healthy side. The change in the direct tract ceases to be visible below the mid-dorsal region, whilst that in the crossed tract can be traced as far as the sacral region. There is no change in the antero-lateral columns, the posterior columns, nor any other portion of the white matter. Marchi stained sections do not reveal any recent degeneration. In sections through the cervical and lumbar enlargements there is an alteration in the motor cells of the anterior horns similar to that found in case No. 1, although in this case such changes are not quite so pronounced. They consist in a diminution in the number of cells composing the lateral and postero-external groups on the right side, and in the same regions the network of fibres is also much less abundant. This diminution in the network is especially pronounced in the middle of the anterior horn, there seem to be as many fibres as usual towards the periphery of the horns. No change can be made out in the mesial-anterior group of cells. The cells of Clarke's column are plentiful, equal on the two sides, and appear perfectly normal.

Case 3.

Atrophy of convolutions of lower part of motor region on left side, and of corresponding efferent tract in pons, medulla and cord. No change in basal ganglia, fillet or cerebellum. Clinically —Right hemiplegia from birth. Epileptiform fits from 12 *years old. Progressive dementia. Death at the age of* 22 *years after severe fits.*

Clinical History.

A. W. was born paralysed on the right side. She had epileptiform fits from 12 years of age, and then began to complain of headache. At the age of 15 mental symptoms made their appearance, and when 18 years of age she had to be sent to the asylum, being then described as dull, listless, and apathetic, with a weak mind and memory, and hesitating speech. She was never able to follow any regular employment. When admitted she had paresis, with wasting of the right arm and leg. Pupils were equal and reacted to light. Knee-jerks were absent. Speech indistinct. No paralysis or affection of the facial muscles. Whilst in the asylum she was subject to constant fits, these began on the paretic side and then became general. She gradually became more and more demented, and died at the age of 22, after a succession of severe fits.

Post-mortem Examination.

The right arm and leg are shorter than the left, there being a difference of one and a half inches between the girth of the calves, two inches between the thighs, and one inch between the forearms of the two sides.

The *Skull* is asymmetrical, the left side being smaller and thinner than the right. There is an opaque thickening of the piâ-arachnoid over the affected area of the brain described below.

Brain.—Weight of left hemisphere 435 grams; weight of right hemisphere 585 grams. There is a small depression in the brain substance at the lower portion of the left motor region, filled with clear fluid and having the thickened piâ stretched over it so as to form a kind of cyst. This depression is due to shrinkage of the lower two-thirds of the ascending frontal and ascending parietal, and the posterior portion of the third frontal convolutions. The left ventricle is greatly dilated. The right hemisphere and all other portions of the brain are normal. No difference exists between the basal ganglia on the two sides.

In the *Pons* there is marked atrophy of the longitudinal bundles of the left side causing considerable asymmetry. No change can be made out in the fillet.

The *Medulla* is also very asymmetrical, the pyramidal fibres on the left side being reduced to a very thin strand. No change can be found in any other region. The olives and the interolivary fillet appear quite normal and of equal dimensions on the two sides.

The *Cerebellum* shows no change whatever. The two halves weigh exactly the same.

The *Spinal cord.*—Sections of the cord were examined at the levels of the second, fifth and sixth cervical, tenth, eleventh and twelfth dorsal, and first lumbar segments. In all these sections it is seen that the right half of the cord is smaller than the left. On careful examination it is quite apparent that this is simply due to diminution of the right crossed pyramidal tract. Under the microscope this area is found to contain fewer fibres and to be the seat of slight interstitial overgrowth of neuroglia. In the cervical region this slight sclerosis extends in the form of a tail-like process almost as far forwards as the origin of the motor roots. In the dorsal and lumbar regions it is confined to the usual triangular-shaped area of the pyramidal tract. In the region of the direct tract there is slight sclerosis and diminution of nerve fibres on the left side as far down as the fifth cervical segment. There is no microscopical change, nor any want of symmetry between the antero-lateral columns, nor the posterior columns, nor any other portion of the white matter of the cord.

In this case, therefore, although the pathological process probably differs from case No. 2, the anatomical site of the lesion is very much the same, and the results on the medulla, cerebellum and spinal cord are practically identical in the two cases.

REMARKS.

It is not proposed to discuss at any length the pathology of these cases. There are probably many causes which may bring about such conditions; but it is likely that vascular occlusion, arterial or venous, is responsible for a large number; and if this takes place before the brain is fully developed it will naturally tend to cause an arrest of development of certain parts, in addition to the actual destruction of nervous tissue produced by the lesion. Case No. 1 may well have been caused by occlusion of a basal perforating artery. Case No. 3 by occlusion of a branch of the sylvian artery (the lesion closely corresponds in its position with the softenings which are frequently found when one of the superior branches of this vessel is blocked). In case No. 2 the affected area almost exactly maps out the distribution of the great anastomotic vein which opens into the superior longitudinal sinus. The atrophy in this case was probably brought about by obstruction of this vein taking place during or shortly after birth; as a result, small necrotic foci occurred, followed later by sclerosis, with atrophy and distortion of the affected convolutions.

There are thus various conditions and many forms in which partial atrophy of one cerebral hemisphere may occur; but the effects resulting therefrom seem to vary considerably with the region of the hemisphere which is affected. In a large number of cases the lesion is confined to the cortex (as in cases 2 and 3), and in such there results a degeneration or arrest of development of the whole, or a portion, of one efferent tract; it is not usually complete, the pyramidal tracts in the medulla and cord still containing some healthy fibres. In such cases there is no change in the cerebellum, fillet, or the antero-lateral columns of the cord.

Several recorded cases of porencephaly instance this, as also do cases of long standing hemiplegia. As long as the lesion is confined to the cortex and does not involve the basal ganglia, the secondary effects are limited to the efferent tracts.

In those cases, however, in which the basal ganglia are involved, the effects are different; although in such the efferent tract is usually affected also, its fibres being involved as they pass through the internal capsule. As a result of this there is atrophy of the white matter of the centrum ovale and of the larger cortical pyramidal cells, with dilatation of the lateral ventricle.

In addition to these changes there is pronounced atrophy in the middle fillet of the pons and medulla, and in the antero-lateral region of the cord on the *same* side as the lesion. There is also atrophy of the superior cerebellar peduncle, and the dentate nucleus, and cerebellar cortex of the *opposite* side.

Many cases of porencephaly, cerebral hemiatrophy, &c., have been already reported in which the basal ganglia were affected, and in most of them this atrophy of the fillet has been noticed, although no special attention seems to have been given to the point.

Such cases have been recorded by Wiglesworth and Campbell (25), Gibson and Turner (7), Norman and Fraser (19), Mahaim (12), Bruce (3), Spiller (23), and many others. In Norman and Fraser's case the interolivary layer on the affected side is said to differ little, if at all, from that on the healthy side; but a series of good photographs of the medulla, which accompany the paper, plainly show that it is but little more than half the size of the opposite healthy one.

Bruce attributed the change in the fillet in his case to atrophy of ascending fibres from the posterior column nuclei, and he states that he found a difference in the size of these nuclei on the two sides. This is the explanation which has generally been considered to account for the condition. One of us (F. W. M.) found atrophy of the posterior column nuclei after unilateral section of the fillet in the monkey (17). In our case, however, the absence of, or, at the most, slight change in the posterior column nuclei, and the atrophy of the antero-lateral column of the cord on the same side, make such an explanation not entirely satisfactory.

In none of the reported cases is there any mention of this atrophy of the antero-lateral column, indeed, in most such cases the cord does not seem to have been examined.

The atrophy in our case is quite definitely marked, and in the case of thrombosis of the middle cerebral artery to which we have referred, there is recent degeneration occupying an exactly similar position. It is, therefore, very desirable that more particular attention should be given to this point in the future examination of such cases, in order to see if the condition is constant in thalamic lesions.

The atrophy of the opposite cerebellar hemisphere in these cases is a well-known fact. It occurred in most of the above-mentioned cases; but we can find no record of the microscopical appearances of this change.

The fact that there is no change in the cerebellum in those cases in which the lesion is confined to the cerebral cortex, shows that there is no *direct* connection between these parts. In such cortical cases of long standing there may be secondary atrophy of portions of the thalamus, but this does not appear to lead to the same changes in the cerebellum and fillet as when the lesion is *primarily* basal.

Case 1 affords a very instructive example of secondary changes dependent upon an anatomical correlation of function, a lesion of the basal ganglia resulting in changes in brain, cerebellum and spinal cord.

Finally, it is very interesting to note that although in these cases the large motor cells of the cortex may be entirely absent, the tangential system of fibres is frequently but little affected. In case No. 2, in which there are practically no large pyramids, there is an abundant network of both tangential and inter-radial fibres, and this in a man who for thirty-three years had been subject to severe epileptic fits. A similar condition also exists in amyotrophic lateral sclerosis, and it may be said that it is only when symptoms of dementia become superadded that we are able to demonstrate atrophy of the tangential system of fibres.

SUMMARY.

It will be well to briefly summarise the chief points of interest in connection with these cases:—

(1) In cases of cerebral hemiatrophy in which the lesion

is confined to the cortex there is sclerosis of the corresponding efferent tract throughout the pons, medulla and cord.

(2) In such cases in which the lesion primarily occurs in the basal ganglia, there is atrophy of the opposite half of the cerebellum with its superior peduncle, also of the mesial fillet in the pons and the interolivary layer in the medulla on the same side, in addition to the sclerosis in the efferent tract.

(3) Corresponding to the atrophy of the efferent tract, there is a numerical diminution in the anterior horn cells of the cervical and lumbar regions of the cord; such diminution being chiefly marked in the cells of the lateral and postero-external groups. In the same regions there is also a numerical diminution of the fibres composing the network within the anterior horns.

(4) As our cases show the cells of Clarke's column to be practically unchanged, the inference is that these cells do *not* form an inter-neuronic connection between the upper and lower efferent tracts.

(5) If the cortical lesion occurs at an early period there is a compensatory increase in the number of large motor cells of the opposite hemisphere.

(6) There may be pronounced atrophy of the fibres of the efferent projection system, and yet the association fibres remain unaltered. Not only may this occur in the brain, but also in the cerebellum.

(7) In the cerebellum there is a layer of granules lying immediately beneath the cells of Purkinje. These are distinct from the granules proper, they are somewhat larger, and are probably connected with an inter-cerebellar association system.

(8) There are fibres passing between the dentate nucleus of the cerebellum and the opposite basal ganglia.

(9) Two of the cases described in this paper point to the existence of a descending path having its origin in the thalamic region, passing thence through the middle fillet of the pons and the interolivary layer of the medulla to the antero-lateral column of the cord on the same side, and descending in this column as far as the lumbar region.

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DESCRIPTION OF THE PHOTOMICROGRAPHS.

FIG. 1.

Brain.—Section of the left occipital cortex stained by Weigert-Pal method. The occipital lobe is practically normal. The white and gray matter and the line of Gennari are well seen.

FIG. 2.

Brain.—Section from a convolution in the left central region, stained by Weigert-Pal method. The outer layer of cells and the line of Baillarger are practically normal. There are, however, no large pyramids, and there is a great diminution of all the nerve-cells below this layer. There are very few large fibres of the projection system in the medullary centre.

FIG. 3.

Cerebellum.—Section across a leaflet of the normal portion, stained by carmine-Weigert method, showing the outer molecular layer, the layer of Purkinje's cells, the inner layer of granules, and the medullary centre containing bundles of large fibres.

FIG. 4.

Cerebellum.—Section across a leaflet of the right lobus culminis, stained by Strœbe's method. This section shows an early stage of atrophy. The outer molecular layer is slightly thinner than normal. The majority of Purkinje's cells have disappeared, but two or three may still be seen. There is considerable diminution in the number of cells forming the inner granule layer, and owing to this, a narrow unchanged zone of outer granules is well seen forming a layer in the situation of the cells of Purkinje. The large fibres are practically absent from the medullary centre.

FIG. 5.

Cerebellum.—A leaflet from the same section as fig. 4, more highly magnified. This shows a still more advanced condition of the atrophy. There are no Purkinje's cells and very few of the inner granules. The layer of outer granules is on this account particularly well seen. There is an almost complete absence of large fibres from the medullary centre.

FIG. 6.

Cerebellum.—A leaflet from the right lobus culminis, stained by the carmine-Weigert method. This section is of the same magnification as figs. 3 and 4, and shows the full extent of the atrophy. The difference between it and fig. 3 is very striking. The outer molecular layer is very much narrowed, Purkinje's cells are entirely absent, and there are very few of the inner granules present. The layer of outer granules is particularly well seen. In the medullary centre there is an absence of large fibres.

FIG. 7.

Cerebellum.—A more highly magnified view of fig. 6. The small granules are seen to be very much diminished, and between this layer and the outer molecular layer are seen fine medullated fibres having a tangential course. There are no. large fibres in the medullary centre, but a network of fine medullated fibres is here plainly visible.

FIG. 8.

Medulla.—Stained by Weigert-Pal's method, showing the atrophy of the left pyramid and interolivary lemniscus. There is also diminution of the left external and right internal arcuate fibres.

FIG. 9.

Spinal Cord.—Fifth cervical segment.

FIG. 10.

Spinal Cord.—Fifth dorsal segment.

FIG. 11.

Spinal Cord.—Tenth dorsal segment.

FIG. 12.

Spinal Cord.—Fourth lumbar segment.

All these sections of spinal cord are stained by the Weigert-Pal method. They show the marked asymmetry of the cord, the left half being considerably smaller. The atrophy of the left antero-lateral column, the huge size of the right direct pyramidal tract, the sclerosis in the right crossed pyramidal tract, and the other points mentioned in the text are well seen.

All the above sections are from Case 1.

FIG. 13.

Brain.—Section from the affected motor cortex of Case 2. Stained by Marchi-Pal method. This shows very well that the tangential, super and inter-radial fibres are present in abundance, although Nissl-stained sections show that there is an almost complete absence of the large pyramidal cells throughout the whole of the motor region of the same side.

FIG. 14.

Brain.—A more highly magnified view of a portion of fig. 13, showing an exceedingly well developed layer of tangential fibres.

A NOTE ON THE DEEP TRANSVERSE FIBRES OF THE PONS.

BY E. E. LASLETT, M.B., B.SC.

Late Demonstrator of Physiology, Univ. Coll., Liverpool; Assist. Med. Officer, Park Hospital, London.

THE lesion on which the following observations are founded was discovered while examining the nervous system of a patient who died from cerebral hæmorrhage. The patient was under the care of Dr. James Barr, at the Royal Infirmary Liverpool, and I am much indebted to him for permission to publish this note.

Although lesions of the pons are not very rare, yet an opportunity of examining the resulting degenerations is comparatively uncommon, and the injury in this instance is an unusually favourable one for the study of the course and relations of the deep transverse fibres.

The pons was hardened in Müller's fluid for a month, and thin slices treated with Marchi's fluid in the usual way. Sections were cut after paraffin embedding.

Lesion.—This is situated in the lower part of the upper half of the pons, about 2 mm. from the median raphe, and so placed as to intercept several large bundles of cross-fibres immediately posterior to the pyramidal tract, and, indeed, to involve to a small extent two bundles of the latter tract. In cross-section it is of an irregularly oval shape, with its long diameter, about 3 mm. in length, transverse. It extends about 2 mm. from above downwards.

It is apparently a softened patch, due most probably to thrombosis of some of the small vessels. There are no signs of hæmorrhage in it, old or recent. Microscopical examination of the softened area shows that it consists of a compact mass of leucocytes, traversed by one or two capillaries; these, as well as the small surrounding vessels, being full of blood. The leucocytes are large, and accompanied by numerous giant-cells, both varieties being filled with granules blackened by the osmic acid.

The lesion is strictly unilateral and does not approach the middle line nearer than 2 mm. at any point, and is, I think, unusually interesting on account of its circumscribed character.

Transverse fibres.—These are degenerated on both sides of the pons, but the altered fibres are much more numerous on the side of the lesion than in the opposite half.

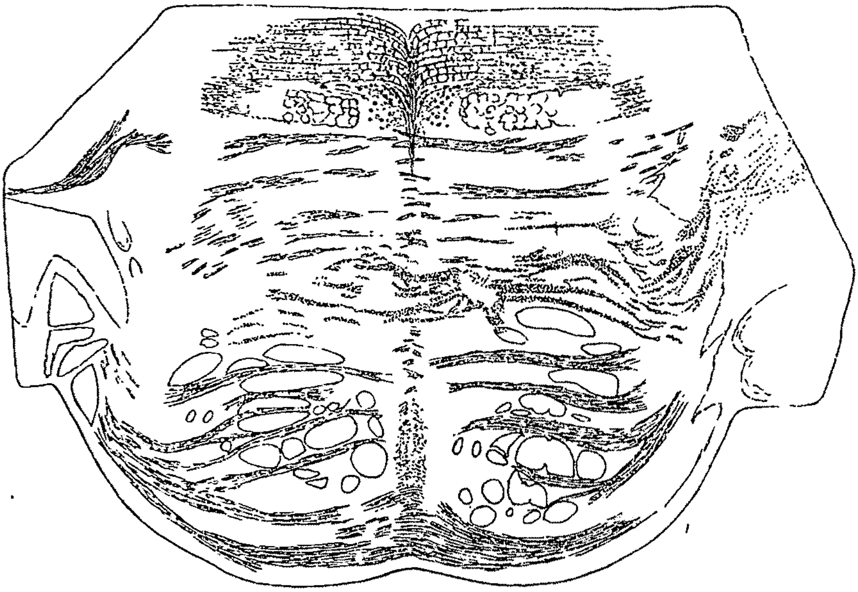

FIG. 2.

A section at the level where the softened area is greatest shows the following features (fig. 2):—(1) On the outer side of the lesion there is heavy degeneration in three main bundles of the cross-fibres, in several minor bundles in the immediate neighbourhood, and also in a thin transverse tract considerably posterior to the main part. Following these tracts laterally, they are seen to break up into smaller bundles, extending over a large area, in the region of the lateral gray matter, and here apparently many of them end. Large numbers of fibres, however, pass beyond the gray matter, and enter in a more or less scattered fashion into the middle cerebellar peduncle, occupying mainly its inner half.

There is also a small degeneration in two of the posterior bundles of the pyramidal tract.

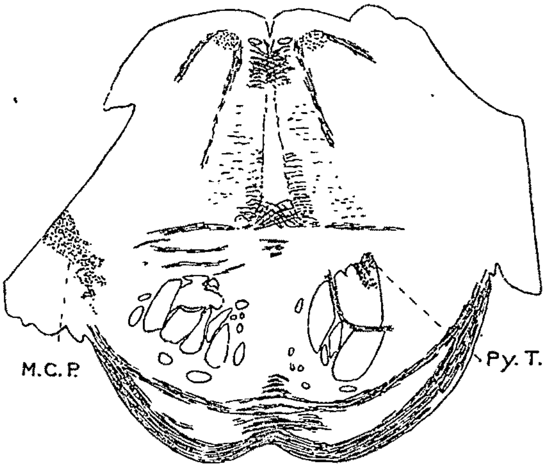

FIG. 1.

Section through the lower limit of pons.

M.C.P.—Degenerated tract in the middle cerebellar peduncle.
Py.T.—Degenerated fibres of the pyramidal tract.

Section at the level of the lesion. The main features are drawn carefully to a magnification of four diameters, so that the area over which the degeneration spreads is accurately represented.

(2) On the inner side of the lesion there is degeneration, also in three bundles. These pass directly to the median raphe, where they cross and have the same course as the above. A few scattered small bundles are seen in the neighbourhood of the raphe some little distance posterior to the lesion. The section from which the figure in the plate was drawn is slightly oblique, and consequently the mode of termination of these fibres on this side is not

shown, but in all respects it is the same as on the side of the lesion.

Sections somewhat above or below this level show the same general appearances, but the number of degenerate fibres diminishes, of course, with the area of softening.

Fig. 1 represents a section through the pons at its lower limit, below the injury. The only descending degeneration is in the posterior part of the pyramidal tract. This is small, and due to the fact above-mentioned, that the softening encroached slightly upon two small bundles of the aforesaid tract. The further course of this degeneration I had not the opportunity to follow. On the opposite side there are still seen some of the cross-fibres remaining, most of which are passing into the middle cerebellar peduncle. The degeneration remaining in the other middle peduncle at this level is too scattered to be represented in the figure.

Sections above the lesion show no degeneration in the fillet or the posterior longitudinal bundle, nor are there any fibres ascending to the corpora quadrigemina.

By studying sections immediately above and below the lesion it is seen that the degenerated transverse fibres are practically confined to the level of the injury, this being an indication that they maintain a fairly horizontal course until they reach the lateral limit of the pons, where, of course, they dip backwards somewhat with the middle cerebellar peduncle.

The lesion from its nature and situation cannot throw much light on the origin of these fibres, but some interesting points as to their destination may be ascertained. Pellizi (1) finds that destruction of the middle lobe of the cerebellum causes degeneration in the median field of the middle peduncle and in the stratum profundum of the pons. According to Cajal ponto-cerebellar fibres spring from the cells of the pontine nuclei. These cross the middle line and pass to the cerebellum by way of the middle peduncle of the opposite side. This is in all probability the origin of many of the degenerated fibres in the present case.

The exact constitution of the middle cerebellar peduncle is not by any means a settled question. Marchi, and Ferrier and Turner found, after destruction of one half of the cerebellum, complete atrophy of the middle peduncle and of all the cross fibres of the pons. Risien Russell states that the latter fibres pass to the pons ganglia of the opposite side.

On the other hand, according to Thomas (2), the above lesion entails degeneration of only a small portion of this peduncle, and he concludes that its fibres are passing from the pons to the cerebellum. Klimow (3) similarly comes to the conclusion that this peduncle consists largely, if not exclusively, of centripetal fibres, originating in a great measure from the pons gray matter of the opposite side with a termination in the flocculus and hemisphere.

The degenerated fibres in the middle peduncle in the present case are, of course, centripetal, and although they are scattered in each section, yet from the depth through which they extend one must conclude that there is a very considerable number of them.

Inasmuch as the lesion is so near the middle line, one may conclude that all the damaged fibres of the same side have really crossed. Nevertheless, one is unable definitely to decide upon the origin of these fibres, which is in all probability a multiple one. Their termination, however, is definitely twofold, namely, (1) in the pons ganglia; (2) in the cerebellum.

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TWO CASES OF ARRESTED DEVELOPMENT OF THE NERVOUS SYSTEM IN CHILDREN.

BY FREDERICK E. BATTEN, M.D.

(1) Arrested development of the left cerebral hemisphere and corresponding pyramid.

(2) Arrested development of the cerebellum with hydromyelia.

Case 1.—A male child, aged six months, was admitted to the Hospital for Sick Children under Dr. Lees, and to him my thanks are due for permission to make use of the clinical notes. When a week old twitching of the left hand and foot were first noticed, when four months old both sides of the body became affected, and for the last fourteen days the child had "gone purple" in the fits. It was the fifth child, all the others being healthy. It was born at the eighth month, and the labour was natural. No evidence of syphilis could be obtained. Its parents were living and healthy.

On admission the child was ill-nourished, weighing 6½ lbs., with a narrow forehead and a markedly asymmetrical head and face, the right side being larger than the left. There was, however, ptosis of the left eyelid and at the same time marked prominence of this eye. The orbicularis palpebrarum acted well.

There was congenital absence of the left thumb.

The trunk and limbs of the child appeared symmetrical, the right arm-jerk was more active than the left, the legs were rigid and the knee-jerks active and equal; no ankle clonus. There was no paralysis of the limbs.

The child had frequent fits, which always terminated by the child sneezing (according to the statement of the sister). During the fits the twitching began on the left side of the face, the eyes were turned to the right, the left leg drawn up, and the left arm flexed, the right leg rigidly extended. The child died a few days after admission to the hospital.

Post mortem.

The asymmetry of the skull was very marked, the prominence of the left eye noted during life being due to the position of the orbital plate.

The left hemisphere of the brain was very much smaller than the right, its substance being hard and firm, the convolutions remaining at the normal development usually reached between the sixth and the seventh month of fœtal life.[1] The right side of the brain was normally convoluted. There was obvious deficiency on the left side of the pons and medulla. The cerebellum was noted as being abnormally large as compared to the size of the brain, being almost as large as that of a child of fifteen months, but there was apparently no asymmetry of the lobes. (No microscopic examination of the organ was made.) All the cranial nerves were normally situated with the exception of the first on the left side, and this may have been torn during the removal of the brain. The eyes were natural, and all the other organs of the body were healthy.

		Right Hemisphere.		*Left Hemisphere.*
Length	..	11·5 cm.	..	10 cm.
Weight	..	5¾ oz.	..	3 oz.

Microscopical examination.—The motor region of the cortex, both on the right and left sides, was examined by Nissl's method. There would seem to be a diminution of the pyramidal cells on both sides, but this diminution was more marked on the left than on the right; the left cortex, however, contained some abnormally large pyramidal cells.

Sections at the level of the corpora quadrigemina showed that the left crus was very considerably smaller than the right. The decussation of the superior cerebellar peduncle was present, and the fibres appeared more abundant on the left side. The posterior longitudinal bundle was well seen and was symmetrical, and the descending root of the fifth was better developed on the right side than the left.

Sections through the pons showed some very marked features; there was almost complete absence of the pyramid on the left side, the fillet on the left side was likewise almost absent, represented only by a very small bundle of fibres, and the superior peduncle of the cerebellum of the right side was very much diminished in size, the left being normal in appearance. The posterior longitudinal bundles appeared symmetrical, and the transverse fibres of the pons also appeared about equal on the two sides.

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[1] RETZIUS. *Das Menschenhirn*, tafe xxviii.

Sections at the level of the eighth nerve showed that the left pyramid was absent, the left fillet was absent, the ascending root of the fifth nerve was equal on the two sides, but the transverse fibres of the pons appeared at this level to be more abundant on the right than the left. This may, however, have been due to the line of the section being somewhat oblique.

At the level of the olive the inferior peduncles of the cerebellum were equally developed, the olivary bodies on the two sides were practically symmetrical, although the right may have been somewhat larger than the left.

At the level of the decussation of the fillet, except for the fact that there was only one pyramid, no other abnormality could be detected. The funiculi gracilis and cuneatus were equal on the two sides.

Spinal Cord.

Cervical region.—The cord to the naked eye appeared almost symmetrical; there was, however, a slight diminution of the white matter on the right side, and under the microscope there was an obvious lack of fibres not only in the crossed but also in the direct pyramidal tract. The central canal in one of the sections was double, and in another was dilated. The grey matter and the cells of the anterior horn appeared normal.

Dorsal region.—The cord in this region appeared normal, except for a slight difference in the size of the white matter on the two sides.

Lumbar region.—The cord in this region appeared perfectly normal.

REMARKS.

One of the most interesting features of the case lies in the fact that the child was not hemiplegic in spite of the non-development of one hemisphere and one pyramid, but the condition found in the cord below the level of the decussation gives the explanation, since both sides of the cord would appear to be innervated from one hemisphere. This has previously been shown to be the case by Russell in a cat, in whom, although both hemispheres were normally developed, there was absence of the right pyramid and the right lobe of the cerebellum. The cord, however, below the decussation appeared normal, and he showed that at the decussation of the pyramid the fibres bifurcated, one set (the larger) passing to the pyramidal tract of the opposite side, while the lesser bundle passed to the pyramid on the same side.

In Russell's case the atrophy of the fillet, superior, middle, and inferior cerebellar peduncles and the pyramid were on the same side. In the present case the pyramid and fillet were atrophied on the same side and the superior cerebellar peduncle on the opposite side, the middle and inferior peduncles being normal. In his case the opposite inferior olive and funiculus cuneatus were atrophied, while in the present case they were apparently symmetrical and normal.

Wiglesworth has also described two cases of porencephaly of one hemisphere with absence of the corresponding pyramid, but in his cases the condition was associated with hemiplegia and descending degeneration in the cord.

Case 2. Arrest of Development of the Cerebellum with Encephalocele and Hydromyelia.

A female child, aged 4 weeks, was admitted to the hospital for Sick Children under Mr. Pitts (to whom I am indebted for the clinical notes) with an occipital encephalocele, which was present at birth, but gradually increased during the first weeks of life. The sac was translucent, and measured 4½ in. round the base. The tumour was removed, and the child did well for eight days, when it died somewhat suddenly.

Post mortem, made twenty-four hours after death. It was found that the meninges passed through a small round hole just large enough to admit the little finger in the occipital bone to form the sac of the meningocele. The hole in the bone was situated in the midline immediately below the torculus Herophili, and it was thus just below the tentorium. The substance of the cerebellum also tapered off, and passed just through the hole in the bone, but probably not further into the sac. The shape of the cerebellum was roughly pear-shaped. The lateral lobes of the cere-

PLATE I.

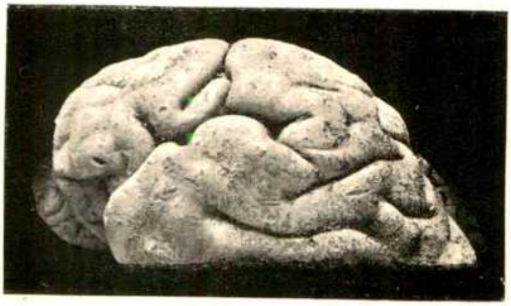


FIG. 1.

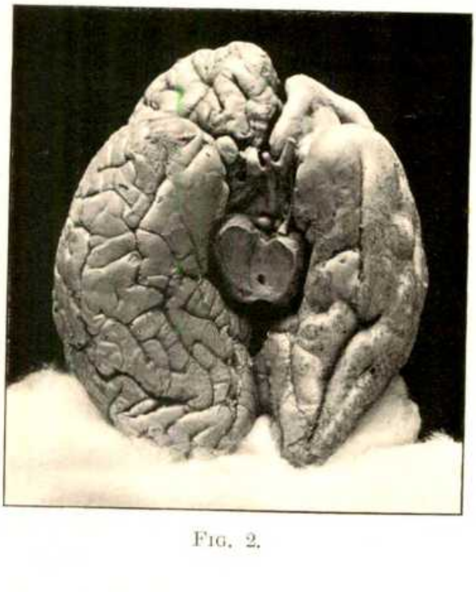


FIG. 2.

bellum were much smaller than normal, and there was some sclerosis in parts. The right lobe appeared rather smaller than the left. The cerebrum was normal to the naked eye, no abnormality, congenital or otherwise, could be detected. The posterior fossa of the skull was curiously deformed, the part below the tentorium being very small and pear-shaped, corresponding to the defective development of the cerebellum.

On the more detailed examination of the cerebellum it was found that the stalk which passed into the cyst was formed of two canals. On passing a probe into the upper one it was found to pass towards the iter, while into the lower one the probe passes into the fourth ventricle. On opening up the canal, however, it is found that they are only separated from one another for a short distance from the point where they are cut off, and both entered the space between the lobes of the cerebellum. The superior peduncle of the cerebellum, which was much smaller than normal, passed back on the dorsal surface of the cerebellum, the lobes of the cerebellum that existed lying wholly ventral to these peduncles. The middle peduncles were normal in situation and in appearance. The inferior peduncle is represented by a small filament which passed up into the wall of the cyst. The two lateral lobes of the cerebellum were completely separated, and it was only the most ventral portion of them that appeared developed. The middle lobe was absent.

Spinal Cord.

The spinal cord at the level of the second cervical was cleft on the dorsal surface, so that the posterior columns were separated from one another by a cavity that was continuous with the central canal of the spinal cord. This cleft extended from the second cervical to the eighth cervical, at which level the cord appeared normal. At the level of the third dorsal, however, a cavity appeared in the centre of the cord, being a dilatation of the central canal. This extended as far as the ninth dorsal, but the greatest amount of dilatation occurred at the level of the fifth dorsal. The lumbar cord appeared normal. The staining was carried out by the Heller-Robertson method. The microscopical examination did not add much to one's knowledge; it proved, however, that the spaces in the cord were true dilatation of the central canal, since they were lined with columnar epithelium. The following is a description of the cord at the various levels:—

Section just anterior to the pons.—At this region the decussation of the superior cerebellar peduncles, the fillet, and posterior longitudinal bundle, appeared normal; the pyramidal tract seen on the ventral side of the section was not well stained.

Section through the cerebellum and pons.—A transverse section was made through the cerebellum and pons. The complete separation of the two lobes of the cerebellum was a very noticeable feature. There was obvious sclerosis of the cerebellar substance, especially on the right side. The fillet, the posterior longitudinal bundles, and the pyramidal tract were normally developed, and the fibres from the inferior cerebellar peduncle were well stained; the transverse fibres of the pons were but little stained.

Section through the medulla in the region of the olive.—The olive was fairly well developed on either side, the interolivary stratum was well stained, the fibres of the inferior peduncle and the ascending root of the fifth were apparently normal. The vagus nerve can be seen normally stained.

Section through the decussation of the pyramid.—At this region the only abnormal feature was the fact that the dorsal median fissure was continuous with the central canal of the spinal cord.

Section at the level of the fourth cervical.—At this level the cord was normal, except for the fact that there was complete separation of the posterior columns, and the dorsal median fissure was continuous with the central canal; the space was lined by epithelium, which proved it to be a true dilatation of the central canal. The tracts and cells of the cord were normal.

At the level of the eighth cervical.—At this level there was no longer a separation of the posterior columns, but there was an abnormal amount of neuroglia tissue situated in the position of Goll's column. The central canal at this region was larger than normal, and had a handle-like projection into the neuroglia tissue in the posterior region.

At the level of the third dorsal.—A triangular-shaped cavity existed, the posterior columns forming a horse-shoe round the neuroglia.

At the level of the seventh dorsal.—The central canal was much dilated, and the posterior columns formed a horse-shoe round the neuroglia tissue, which was present on the dorsal side of the central canal.

At the level of the first lumbar.—At this level the cord has assumed its normal appearance.

PLATE II.

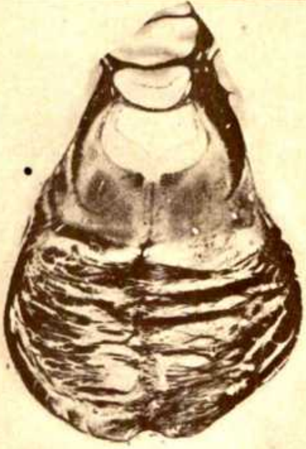


FIG. 1.

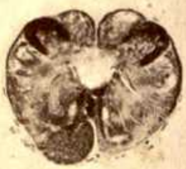
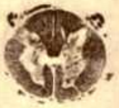


FIG. 4.



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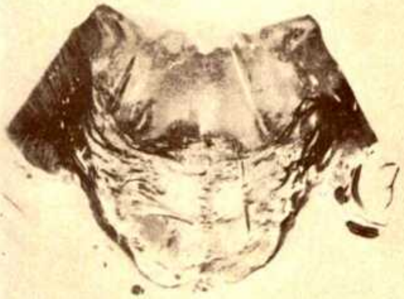


FIG. 2.

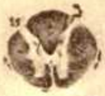


FIG. 6.

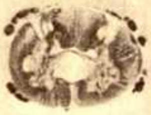


FIG. 5.

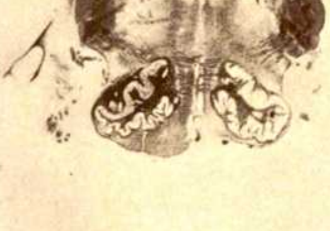
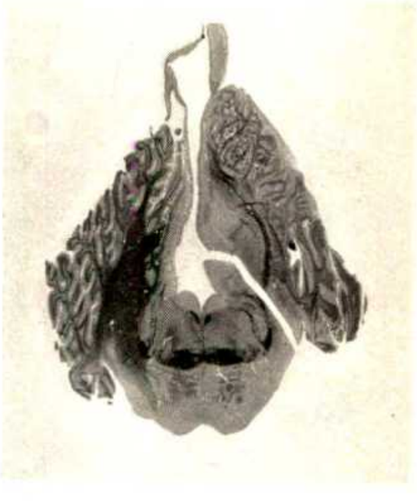


FIG. 3.

PLATE III.



REMARKS.

The abnormality met with in this case would seem to be that which is usually found in cases of occipital meningocele, *i.e.*, lack of development of the cerebellum, the cyst communicating with the fourth ventricle. Two canals, as in the above case, have been described as passing through the opening in the skull.

A similar case was described by Sutton in his "Tumours," and the specimen is said to be in the museum of the Middlesex Hospital. In this case there was said to be no cerebellum, but the flocculus was large and conspicuous. He also points out that the flocculus is developed from lateral outgrowths from the floor of the third vesicle, while the cerebellum is developed from the foremost part of the roof of that vesicle.

Leyden also described two cases of meningocele in the occipital region, with absence of the cerebellum and dilitation of the central canal in the cervical and dorsal regions, the first case being that in a child two and a half years old and the second in a child two years old.

REFERENCES.

(1) RUSSELL. BRAIN, vol. xviii., p. 37, 1895.
(2) WIGLESWORTH. BRAIN, vol. xx., p. 88, 1897.
(3) SUTTON. "Tumours," p. 452.
(4) LEYDEN. *Virchow's Archiv*, Bd. lxviii., plate I., p. 1.

DESCRIPTION OF PLATES.

PLATE I.

FIG. 1.—Lateral view of left cerebral hemisphere of child, aged 6 months, showing arrest of development at about the sixth to seventh month of fœtal life. (Comp. Retzius, *Das Menschenhirn*, tafel xxviii.

FIG. 2.—Ventral aspect of the same brain, showing the marked asymmetry between the two hemispheres, and also the lack of development of the left crus.

PLATE II.

FIG. 1.—Section through pons of same case, showing absence of left pyramid, left fillet, and diminution in size of right superior cerebellar peduncle.

FIG. 2.—Section at the level of the eighth nerve, showing absence of left pyramid and left fillet.

FIG. 3.—Section at the level of the olive, showing the absence of left pyramid, the symmetry of the olives and of the inferior peduncles of the cerebellum.

FIG. 4.—Section at the level of the decussation of the fillet, showing the absence of the left pyramid and the symmetry of the funiculi gracilis and cuneatus.

FIG. 5.—Section of cord in cervical region, showing that the right side of the cord is smaller than the left, and there is some dilatation of the central canal; it can also be seen that the fibres in the direct pyramidal tract of the left side and the crossed pyramidal tract of the right side are not medullated.

FIG. 6.—Section of cord in dorsal region; the asymmetry is less marked than in the cervical.

FIG. 7.—Section of cord in lumbar region; the asymmetry of the cord is very slight, the right side being slightly smaller than the left.

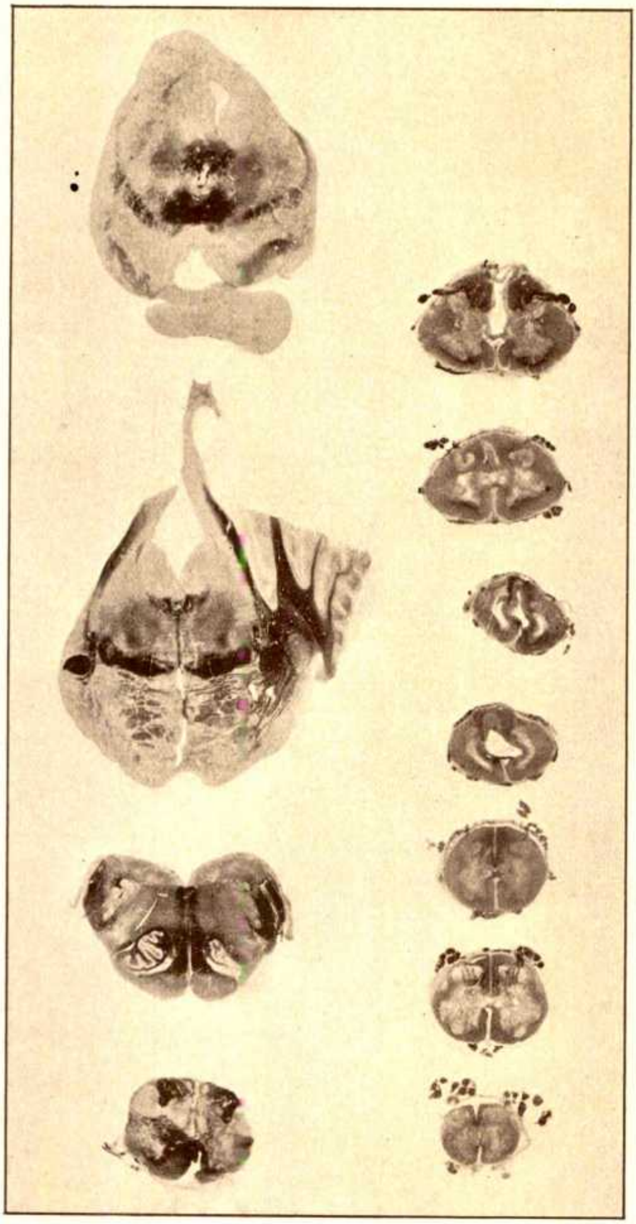
PLATE III.

Section through pons and cerebellum of child, aged 4 weeks, with occipital encephalocele, showing complete separation of the lobes of the cerebellum, with sclerosis of the right. The middle lobe is absent. (The cut separating the right lobe of the cerebellum from the pons is artificial.) The cavity between the two lobes communicated with the cyst in the occipital region.

PLATE IV.

Sections at various levels through the pons, medulla, and cord, showing the separation of the posterior columns in the cervical region and the dilatation of the central canal in the dorsal region, and the normal appearance of the cord in the lumbar and sacral region.

PLATE IV.



Critical Digest.

MYASTHENIA GRAVIS.

BY

HARRY CAMPBELL, M.D., F.R.C.P.

AND

EDWIN BRAMWELL, M.B., M.R.C.P.

THE disease known as myasthenia gravis has hitherto attracted little attention in this country. Nevertheless some sixty cases have been recorded within the last few years, chiefly by German writers, and the disease has found a recognised place in German text-books on neurology.

We have ourselves had the opportunity of examining nine cases.

The disease has received various names. The earlier cases were published as "cases of bulbar paralysis without discoverable anatomical changes," and some recent writers have adopted this nomenclature. Strümpell introduced the term "Asthenic bulbar palsy." The affection is, however, not confined to the bulbar muscles. Other names which have been employed are "general profound myasthenia," "Erb's disease," the "Erb-Goldflam" and the "Hoppe-Goldflam-symptom-complex." Jolly has proposed the term "myasthenia gravis pseudo-paralytica," and this, or for short "myasthenia gravis," appears to us the most suitable and convenient hitherto suggested.

SALIENT FEATURES OF THE DISEASE.

There is weakness, sometimes amounting to complete paralysis, of some or all of the voluntary muscles. After prolonged rest of the affected muscles, *e.g.*, the first thing in the morning, they may respond normally to the will, but they become rapidly exhausted after voluntary contractions, regaining their power again after rest. In severe cases, however, weakness and, indeed, actual paralysis may persist even after prolonged rest.

The affected muscles often exhibit the "myasthenic reaction," becoming exhausted by faradic stimulation just as they are by voluntary effort; galvanism, on the other hand, having little power in this respect.

The entire system of voluntary muscles may be affected, but those muscles are most apt to be implicated which normally act most constantly, such as the cervical muscles and the extrinsic muscles of the eye-balls. The bulbar muscles are very generally involved. Hence the term "asthenic bulbar paralysis."

A characteristic feature of the disease is its tendency to fluctuate in severity from day to day, or from week to week, or even to disappear for months or years, to reappear.

There are no sensory symptoms. Death occurs in a large proportion of the cases, but no structural changes have been discovered to account for the symptoms.

HISTORICAL.

Wilks (1), in a paper published in *Guy's Hospital Reports* for 1877, describes a case of bulbar paralysis in which no anatomical changes were found after death. This is the first reference to myasthenia gravis to be found in the literature.

Erb (2), in the following year, described a peculiar form of bulbar disease ("einen eigenartigen wahrscheinlich bulbären symptomen complex"), the characteristic symptoms of which were: ptosis, weakness of the jaws and neck muscles; and of secondary importance—weakness of the tongue and extremities, difficulty in swallowing, and weakness of the upper part of the face.

The publications of Wilks and Erb do not appear to have attracted much attention, for no further publication followed until 1887, when two cases were recorded, the one by Oppenheim (5), the other by Eisenlohr (4). In 1890 two cases were described by Bernhardt (7) and Leonard Shaw

(6), but it was not until the papers of Jolly (8), Hoppe (11), and Goldflam (9) appeared, that the disease was established as a definite clinical entity.

Hoppe, in 1892, was the first writer to give a full account of the disorder.

In 1895 Strümpell* reviewed the literature of the disease and collected twenty undoubted examples which had been reported up to that time. In 1898 an excellent *resumé* of the subject appeared by Laquer (40) of Frankfort.

During the last four or five years there have been numerous additions to the literature of the disease, and there are now some sixty or seventy cases on record, ten having been described in this country. †

The most complete account of the disease published in this country is that of Buzzard (55).

Of the cases hitherto recorded ten have been in England, four in America, eight in France, five in Italy, the remainder in Germany and Austria.

It is difficult at present to form an idea as to the frequency of a disease the clinical picture of which is so little known to the medical profession. The condition is undoubtedly a rare one. Erb did not meet with another case for twenty years after his original description.

During the last six months four patients suffering from myasthenia gravis have been treated in the National Hospital, Queen Square.

ETIOLOGY.

Males and females are almost equally affected. The age at which the sexes are attacked is different. Of fifty-eight cases the average age was for men 35 and for women 24 years. The youngest patient in whom the disease has been observed—excluding a doubtful case in a child aged 2½ described by Mailhouse, (39)—was 12, the oldest patient, 55.

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* Strumpell's cases :—
Wilks (1)
Oppenheim (1)
Jolly (2)
Reinak (1)
Erb (3)
Shaw (1)
Goldflam (4)
Pineles (3)
Eisenlohr (1)
Bernhardt (1)
Hoppe (1)
Strümpell (1)

† Wilks (1)
Suckling (2)
Harry Campbell (1)
Shaw (1)
Clifford Allbutt (1)
Buzzard (2)
Dreschfeld (1)
Guthrie (1)

With regard to occupation, no conclusive deductions are to be drawn, although in the majority of instances in which mention of this point has been made the patients have been manual workers.

Rarely has there been a family tendency to nervous disease. Exceptions to this are found in cases recorded by Goldflam (9), Sinkler (50), Buzzard (55), Suckling (15), and Kojewnikov (30). No case is on record in which more than one member of a family has been affected. As frequently as not the malady attacks individuals who have previously enjoyed good health. A considerable percentage of the female patients have been anæmic. Laquer's patient suffered from attacks of gout. In a few instances there have been signs of a defective nervous system. In Berkeley's (34) case there was an obvious mental defect. In a case described by Karplus (37) the patient had recurring ptosis from the time she was 5 years of age. In Saenger's (43) case the patient had infantile paralysis when a child. Eisenlohr's patient as a child suffered from megrim occasionally accompanied by ptosis. With these exceptions there is a striking absence of a nervous or hysterical temperament.

Syphilis and alcohol appear to play no part as causative factors.

Not infrequently the symptoms have followed upon some previous affection, such as influenza (Remak, 12), scarlatina (Campbell, 53), typhoid fever (Sinkler, 50), sore throat (Saenger, 43; Eulenberg, 38), otitis media (Jolly, 20), an attack of diarrhœa (Shaw, 6), and acute intestinal obstruction (Feinberg, 57). In one case the onset of menstruation (Kojewnikov, 30), in others a confinement (Punton, 51, Laquer, 40), appear to have acted as exciting causes. Emotional excitement (Angelini, 49), a chill (Kojewnikov, 30; Clifford Allbutt, 53), the extraction of a tooth (Wheaton, 41) and an attack of megrim (Eisenlohr, 4) have been blamed. In two cases the illness was attributed to taking cold baths (Buzzard, 55; Montesano, 45), in others to over-exertion (Suckling, 15, Buzzard, 55).

MODE OF ONSET.

The disease usually comes on gradually, although in a few cases the onset has been sudden. Occasionally slight headache, pain in the neck and back, giddiness and photophobia have immediately preceded the first symptoms of motor weakness.

Most frequently the characteristic weakness first shows itself in the muscles innervated by the bulb. Thus, in the case of a schoolboy, the first symptom was an inability to keep the eyes open—he was unable to look at the blackboard on account of the dropping of the upper eyelids. Diplopia, weakness of the lips, indistinct speech, difficulty in masticating and in swallowing, and inability to hold the head erect, have each been met with as the earliest manifestations of the disease. A considerable number of cases have been described in which the limbs were first affected. An hotel cook found that his fingers were weak after rolling dough. Another patient first noticed weakness in the fingers after sawing wood. A housemaid, who had a great deal of "stair work," became very weak in the legs, so much so that on several occasions the legs gave way and she fell to the ground. In some cases the initial weakness is more general, affecting both the limbs and bulbar muscles.

SYMPTOMATOLOGY.

Bulbar muscles.—Ptosis is a common symptom; it is usually bilateral and often more marked on one side than the other. Sometimes the ptosis is constant; in other cases it is only present towards the latter part of the day, or if the patient attempts to look up for any length of time, when the upper lids gradually fall. On account of weakness of the occipito-frontales muscles, frontal overaction, which is so frequently associated with the ptosis of tabes and serves to antagonise the drooping of the lids, cannot occur. The only way in which the patient can counteract the ptosis is by throwing back his head, but here again weakness of the neck muscles makes it difficult for him to maintain this position.

Some interesting observations in connection with ptosis were made in Dr. Buzzard's male case. It was observed by Mr. Marcus Gunn that on appealing to the patient's emotions and occasionally upon mental concentration, the upper lids were temporarily raised to some extent, in association with a certain amount of dilatation of the pupils. In the same patient on another occasion, just after he had awakened from sleep, the upper lids were retracted so that the sclerotic was visible above the corneal margin. In this, as in several other recorded cases, von Graefe's sign was at times present. These facts would suggest that the fibres of Müller are not affected.

Weakness of the external ocular muscles with consequent diplopia is often present. Sometimes one muscle is more affected than others, sometimes there is a general paresis affecting all the extrinsic muscles, while in some cases complete and persistent ophthalmoplegia externa has been present. A striking feature of the diplopia in myasthenia gravis is the alteration in the relative position of the two images at different times.

In some cases irregular nystagmoid movements, similar to those seen in conditions of general asthenia, are induced upon conjugate lateral deviation of the eyes. The ocular muscles, as is the case with other voluntary muscles, become readily fatigued; patients frequently complain that after reading a few lines the letters and words become blurred and indistinct, and run into each other.

Pupil changes are quite exceptional. The pupils are sometimes unequal. In one case, recorded by Brissaud and Lantzenberg (36), in which, however, the diagnosis appears doubtful, they did not react either to light or accommodation, while in one or two others the reactions were sluggish.

In Dr. Buzzard's case, already alluded to, after prolonged convergence the pupils showed a great tendency to oscillatory movements. Attempts to tire out accommodation in this case, as in others in which the experiment has been tried, were unsuccessful, nor was it found possible to exhaust the sphincter iridis by holding a bright light in front of the eyes.

Difficulty in masticating is one of the most constant symptoms of the disease. The difficulty may be slight and only noticeable after a meal, and more especially towards evening. Sometimes the weakness of the muscles of mastication is so great that the finger may be placed with impunity between the patient's teeth while he closes the jaws with all the force he can command. Often the mouth is kept slightly open because of the weakness of the elevators of the jaw. In cases in which the weakness of the muscles of mastication is great, there is a tendency for the lower jaw to drop, which causes great distress to the patient. In several cases the patient was in the habit of supporting the lower jaw with the hand while masticating.

In Buzzard's first case a curious symptom, connected with the jaw muscles, was complained of. The patient stated that not infrequently he was wakened from sleep by a champing movement of the jaws, which sometimes resulted in his biting his tongue. This symptom was probably due to a clonic contraction of the elevators of the jaw, and is comparable with the clonic movements which have been occasionally noticed in the extremities. Patients sometimes complain of an increased flow of saliva, probably comparable to the well-known dribbling of bulbar paralysis.

The facial appearance is striking and characteristic. The immobile, expressionless face and the drooping upper lids remind one of the Landouzy-Dejerine form of myopathy. Often there is complete inability to wrinkle the forehead, raise the eyebrows, or to frown. Erb (2), in describing his early cases, draws attention to this upper facial weakness.

The sphincters of the orbit are often so weak that the patient is unable to keep his eyes closed against the slightest resistance. In many cases there is great weakness in the muscles about the mouth. A very poor attempt is made to raise the upper lip and show the teeth; the patient cannot pout the lips, "empty a spoon with the upper lip," whistle, or blow out a candle. In extreme cases fluids dribble from the mouth while drinking. In one case the patient was in the habit of supporting the lower lip with her fingers to prevent this occurring.

Difficulty in swallowing is another symptom which is rarely absent. In several instances death has followed attacks of choking brought on while swallowing. Fluids are, as a rule, more easily taken than solids, although, on account of weakness of the palate, they frequently regurgitate through the nose. One patient, when swallowing, always supported the hyoid bone with her hand. The pharyngeal reflex is often absent, a fact which is probably of importance in explaining this symptom.

Weakness of the palate is of frequent occurrence, the voice becomes nasal, and, if the weakness is marked, fluids regurgitate through the nose when the patient drinks. The patient is unable to blow out his cheeks, the air escaping through the nose. The movement of the palate is almost always impaired and becomes much more feeble after repeated vocalisation of the letter ā.

The palatal reflex is usually diminished, and may be absent.

Paralysis of the laryngeal muscles has been but rarely noticed. In one case there was paralysis of one vocal cord (Punton, 51); in another movement of one cord was defective (Bernhardt, 7). In other cases the tone of the voice has been lowered, suggesting weakness of the adductors.

In Hoppe's case there was weakness of both abductors and adductors. In one case (Dreschfeld, 14) the abductors, in another the adductors were weak (Kojewnikov, 30). In Dr. Buzzard's first case it was remarked by Sir Felix Semon that after repeated deep respirations the cords did not separate so much as at first, clearly showing myasthenic weakness of the abductors. In two cases, those of Wernicke (16) and Toby Cohn (31), anæsthesia of both pharynx and larynx was present.

A feeling of fatigue and of "aching" and "stiffness" in the tongue is often complained of, especially after speaking or eating. The movements of the tongue may be impaired. The patient can usually protrude the tongue, but cannot long maintain it in this position, and he may not be able to thrust out the cheek forcibly with it.

Very characteristic alterations in speech occur. It may be that the patient speaks naturally when he begins, but soon speech becomes nasal; words become more and more indistinct; the voice becomes weaker and weaker, and finally he has to stop for want of breath. The altered speech is due, in part, to weakness of the articulatory apparatus—lips, jaws, tongue, and soft palate; in part to defective action of the respiratory muscles, which make it impossible for the patient to take in sufficient air for phonation. These peculiarities are well demonstrated when the patient reads aloud.

Trunk muscles.—The myasthenia, as already observed, involves the muscles of the trunk and limbs, as well as those just considered.

Weakness in the neck muscles and consequent inability to support the head is common. In some cases the head tends to fall forwards, in others backwards, and it often requires support.

The muscles of the back may suffer in a similar manner, so that the patient cannot sit up for any length of time without feeling tired. On account of weakness of the abdominal muscles he may be quite unable to raise himself from the recumbent to the sitting posture without using his hands. So marked is the weakness of the trunk and limb muscles in some cases that there is the greatest difficulty in turning in bed.

The muscles of respiration may likewise be involved. In one case the difference between the circumference of the chest at full inspiration and complete expiration amounted to a quarter of an inch only. The dyspnœa, which results on even slight exertion, finds a ready explanation in this fact. Besides the dyspnœa which follows exertion, unaccountable attacks of breathlessness occur, during which the patient is in danger of his life. Strümpell (24) gives a graphic account of the dyspnœic attacks which occurred in his case:—"The patient falls to the ground if walking, becomes cyanosed and breathless. Respiration is noisy and restless; sputum accumulates in the mouth; he can neither swallow it nor spit it out. The tongue appears to sink back into the mouth. If in bed he sits up with head bent forwards, the saliva flowing from his mouth. The arms when raised fall flaccid to the side." These attacks may persist for several hours. Strümpell believes that they are due to sinking back of the tongue, and in his case he was in the habit of pulling the tongue forward with marked benefit. Attacks of palpitation are not uncommonly complained of, sometimes in association with dyspnœa, at other times quite independently. The palpitation may be entirely subjective and unassociated with any increase in the pulse rate.

Extremities.—It has been pointed out that in the extremities the muscles situated near the trunk usually suffer most. Not infrequently the first weakness in the arms is noticed when the patient undresses at night to go to bed. One of the earliest symptoms in the case of a female patient was inability to raise the arms in order to brush her hair. But the weakness is by no means confined to the shoulder and upper arm muscles. In two cases, already referred to, weakness in the fingers was the first symptom to appear. The handwriting may show characteristic changes dependent upon the myasthenic condition. At first the letters are well formed and the patient writes fairly rapidly, but gradually the writing becomes slower and more laboured and the letters badly formed, until finally he has to give up the attempt. Weakness in the arms may be so great that the patient cannot feed himself. The ilio-psoas and quadriceps would seem to be the muscles which are as a rule most involved in the legs. As a rule the patient is unable to walk a long distance, sometimes he cannot walk fifty yards, indeed, he may not be able to walk at all.

In slight cases the patient appears to walk quite naturally. When the legs feel tired he rests for a minute or two, and then walks on almost as well as before. In cases in which the lower extremities are very weak the gait is waddling in character.

Sudden giving way of the legs is a not infrequent symptom, and was first drawn attention to by Strümpell.

Factors influencing the myasthenic condition.—Emotional excitement increases the intensity of the symptoms in a very striking way. In one of Goldflam's cases a relapse occurred after a fright. The presence of a strange doctor may be sufficient to intensify the symptoms for the time being. In one case reading an exciting description of a battle produced a similar result.

Buzzard's patient always felt worse in cold weather. In a case under the care of Dr. Ormerod five years ago, which presented many of the features of myasthenia gravis affecting the limbs, the patient, a blacksmith, writes to say that he is now quite well, although in the cold weather he still notices some weakness in his fingers. The myasthenia in Campbell's second case was always increased by cold weather.

Female patients are often worse at the menstrual periods. Such was very decidedly the case in one of our own patients. As we have seen, several of the recorded cases have come on after a confinement.

The speedy production of muscular exhaustion constitutes the most striking feature of the disease. Persistence in a movement causes it to become gradually weaker, and ultimately impossible, until after a short rest, when it can again be repeated.

As Strümpell pointed out, persistent paresis picks out especially those muscles whose function necessitates persistent activity, such as the cervical muscles and the extrinsic muscles of the eyes.

Laquer (40) found that fatigue induced in one group of muscles causes fatigue in others, and Mosso has shown that this is also true of physiological fatigue. Goldflam, on the contrary, in a case which he examined, was unable to demonstrate this point. Observations on Dr. Buzzard's cases support Laquer's conclusion.

The great variations which occur in the intensity of the symptoms from time to time are very characteristic of the disease, and were first called attention to by Goldflam (13). Even in hospital, when a most careful record is kept of a patient's every act, quite unaccountable relapses occur.

Electrical reaction.—Jolly (20) in 1895 drew attention to the peculiar manner in which the muscles react to electrical currents. He found on applying a tetanising current to the muscles of a patient suffering from this disease a brisk contraction was produced, but that if the electrodes were kept in contact with the muscle the contraction became gradually feebler until finally the muscle ceased to respond. On removing the electrodes and reapplying them again after a minute or two a good contraction was obtained, which disappeared just as on the first occasion. Jolly compared the exhaustion produced by electrical stimulation to that which results after voluntary exertion, and he gave the name *myasthenic reaction* to the phenomenon which he had observed.

The myasthenic reaction is not always present; it occurs in some cases as a passing symptom, in other cases it has not been obtained.

At one time a muscle can be exhausted in twenty-five to thirty seconds by the application of a moderately strong current, at another time it is impossible to exhaust it; a fact not surprising in view of the known variability of the myasthenia from time to time. The comparison between the myasthenic reaction and the myotonic reaction found in Thomson's disease is of interest.

Further, the myasthenic reaction is met with in different muscles at different times.

Murri (25) made the interesting observation that after a muscle has ceased to respond to the faradic current voluntary power still persists, and is only slightly diminished in degree.

The readiness with which the myasthenic reaction can be obtained, as Jolly has remarked, varies with the degree of fatigue in the muscles.

Attempts to exhaust the muscles with galvanism result only in a slight diminution in the contraction.

In cases described by Erb (2), Oppenheim (5), Bernhardt (7), Senator (10), Kojewnikov (30), Montesano (45), Wernicke (16), Pineles (23), and Kalischer (32) diminished excitability was present in certain muscles, notably in those of the tongue, neck, and shoulder. In Kojewnikov's case reaction of degeneration was present in the tongue.

Atrophy.—Although muscular atrophy is altogether exceptional in this disease, in a few cases it has been met with. Some of the recorded instances have probably been cases of polio-encephalitis (superior nuclear palsy), but others—and such cases are of extreme interest—have presented the classical features of myasthenia gravis.

In one of Erb's cases the masseters were atrophied. Atrophy of the tongue has been described by Erb (2), Dreschfeld (14), and Kojewnikov (30). In Dreschfeld's case there was some degree of atrophy in the sternomastoids, trapezii, and deltoids. In Kojewnikov's case the face muscles were manifestly atrophied, while both masseters, especially the left, were very atrophic.

In Kostetzki's (47) case the pectorals, deltoids, thenar and hypothenar eminences, glutei and spinal muscles, were atrophied. In this case, however, the diagnosis was not quite clear, the writer regarding it as a transition form between chronic bulbar paralysis and asthenic bulbar paralysis. One of Laquer's (40) cases is of the greatest importance in this relation, for in it atrophy of the deltoid, biceps, triceps, pectorals, interossei, quadriceps, and calf muscles, developed while the patient was under observation.

Fibrillary contraction was present in the tongue in cases recorded by Erb (2) and Senator (10), but in no other region has it been noticed.

In some cases occasional chronic spasmodic jerks occur in the extremities; this was so in Buzzard's female case (55).

The muscular sense and co-ordination are never impaired.

With the exception of a feeling of fatigue in the muscles after they have been exercised, and of stiffness due probably to immobility, sensory symptoms are seldom present. Sometimes patients complain, even when lying in bed, of an aching in the limbs, and this, like the stiffness, is probably connected with the immobility of the affected parts. The muscles are sometimes tender on pressure; no other objective sensory disturbance occurs.

The skin reflexes are in no way peculiar. A jaw-jerk is sometimes present. The triceps- and biceps- jerks are, as a rule, brisk, although in some cases it is difficult to elicit them.

The knee-jerks are usually rather more active than normal. In a case described by Collins (26) it was found possible to abolish the knee-jerk by seven or eight strokes on the patella tendon. In one of Goldflam's cases a similar condition was present, while in Strümpell's case the activity of the knee-jerk appeared to diminish somewhat. In other cases the knee-jerk did not diminish after repeated tapping (Laquer, 40; Angelini, 49; Buzzard, 55). The knee-jerk does not diminish if the quadriceps is fatigued. In one of Buzzard's cases exhaustion of the vastus internus by faradisation produced no effect on the knee-jerk. Ankle clonus is not met with. The plantar reflex, where it has been tried, gives a flexor response.

The sphincters are never affected in this disease. No trophic changes occur in the bones or skin.

Morbid Anatomy.

In the great majority of cases in which an autopsy has been made no lesion has been found.

Of seventeen cases which have come to the *post-mortem* table, in only six was anything abnormal found which could *possibly* account for the symptoms, notwithstanding that in many of the cases the most modern methods were used, and the microscopical examinations made by highly skilled observers.

Two cases described by Mayer (18) and Kalischer (32) respectively, deserve special attention in this relation. Mayer's case appears to have been an undoubted example of the disease. The patient had speech trouble, difficulty in swallowing, weakness of the jaw muscles, double ptosis, and paresis of the extremities; there was no atrophy, and the reflexes were normal; towards evening and after exertion all the symptoms were most pronounced; temporary improvements and relapses occurred, death ultimately occurring by choking. Microscopical examination showed that the cells of the hypoglossal nucleus, with the exception of a small number which contained vacuoles, were completely normal, as were those of the anterior horns. A morbid condition of the intra-medullary portion of the anterior roots, as well as the hypoglossal root, was present, particularly well seen in Marchi preparations. Undoubtedly the condition of the nerve sheaths was pathological, but to what extent the axis-cylinders were affected could not be determined.

In the case which Kalischer describes, the diagnosis is not absolutely certain. Jolly (20) believes it to have been a case of myasthenia gravis, but Strümpell (24) is not convinced. A description of the case will be found in the appendix. Kalischer found degenerative changes in the cells of the motor gray matter from the oculo-motor nucleus, through the whole length of the cord to the sacral region, the fine fibres of the gray matter being rarified. Small hæmorrhages were seen round the dilated blood-vessels in this region. The vessels had in places undergone changes, the adventitia was thickened, and here and there aneurismal dilatation of the lumen was present.

Widal and Marinesco (33) have recorded a case in which, besides dilatation of the vessels, a partial disappearance of the chromatophilic elements in the nerve-cells of the third, sixth, seventh, and twelfth nuclei existed. Degenerated fibres were demonstrated by the Marchi method in the third, seventh, and twelfth nerve-roots. This case again is not quite typical, for death, which occurred suddenly fourteen days after the first symptoms were noticed, was preceded for eight days by slight fever.

In a case reported by Murri (25), numerous hæmorrhages were present and chromatolysis in some of the cells of the hypoglossal nucleus. Cohn disregards the cell changes found in this case, since the *post mortem* was not made until six days after death.

In two cases (Eisenlohr, 4; Wernicke, 16), recent hæmorrhages were found in the medullary nuclei. These patients died, the one of paralysis of the diaphragm, the other suddenly of asphyxia, and it is possible that the hæmorrhages were produced in the act of dying. In another case, described briefly by Charcot and Marinesco (22), in which recent hæmorrhages were met with beside the aqueduct of Sylvius and about the ventral nucleus of the vagus, the patient died with "bulbar symptoms."

Such cases are, however, exceptional, and, as already observed, in the majority of cases no visible lesion has been met with after death. In the few cases in which changes have been present, these changes, as Kalischer (32) and Laquer (40) have pointed out, were not present in all those centres whose functions showed signs of disturbance during life. Changes, no doubt, are present, although it may be that they cannot be demonstrated by our present methods; but it is open to question whether those hitherto described are actually the cause of the symptoms which the patients manifest during life. It is of great importance that in future careful examination be made not only of the multipolar cells, but also of the muscles themselves, of the nerve-endings in the muscles, of the motor nerves, nerve-roots and cortical cells.

In the few cases in which the muscles have been examined no changes have been found.

SEAT OF LESION.

It can be readily understood that in the presence of such a meagre morbid anatomy, various views are held as to the seat of the lesion.

As Strümpell states (24), there is not a single case which is associated with symptoms pointing to parts other than the motor nervous system, and so much seems to be admitted by all observers. Collins (26), although he admits that the phenomena of the disease are largely manifested through the motor system, is inclined to regard the condition as due to an affection of the sympathetic. He bases his opinion upon the attacks of collapse and cyanosis from which his patient suffered.

Jolly (58) concludes from the myasthenic reaction that an abnormal condition exists in the muscles themselves. There are, he contends (58), no certain facts proving that the disease is one of the central nervous system.

Mendel (58) thinks that the occurrence of sudden death in some cases is opposed to the view that the disease is always a purely muscular affection. Strümpell (24) argues from the myasthenic reaction that the affection is not limited to the upper motor neuron.

It is not possible, with the facts we at present possess, to make any definite statement as to the part or parts of the neuromotor apparatus involved by the morbid process.

PATHOLOGY.

We are equally ignorant as to the true pathology of the disease. It has been suggested, and this view is very generally accepted, that the disease is due to some toxic agent, the result of a disturbed metabolism. Laquer strongly supports this metabolic theory, and he points out with regard to physiological fatigue that the preservation of normal muscle excitability is dependent upon a suitable change between rest and activity, that long-continued activity, resulting in the complete loss of irritability, is the condition in fact which we call fatigue, and that the appearance of fatigue depends upon the existence of products of decomposition out of the muscle substance itself which accumulate in the blood.

Collins (26) thinks that the most plausible theory of the pathogenesis of the disease is that a poison is generated in the system and continuously operates on the vegetative portion of the body. When vitality is sufficiently low to let the poison get the upper hand a relapse occurs.

It may be, however, that the toxine is of exogenous and not of endogenous origin. As Strümpell points out (24), the absence of any family tendency and the onset in some cases after an acute illness are in favour of this view.

In regard to the pathology of the disease it is impossible at present to do more than surmise. The view we ourselves put forward is that the disease is due to a poison probably of microbic origin acting upon the lower motor neurons and interfering with their functional activity without necessarily producing discoverable change in structure. We suggest that the poison acts upon the motor fibre (= axon) or end plates; as to whether it also acts upon the cell-body (in bulbar nuclei or anterior horns), we can form no opinion.

The evidence in favour of a toxine being the pathogenic agent is strong. The symmetry of the affection is alone highly suggestive of this view; also the fact that it occurs in connection with disease in which nerve poisons are known to be produced. Thus cases occur after such diseases as scarlatina, influenza, sore-throats, typhoid fever, which are well known to be often followed by toxic neuritis. Other cases have occurred after otitis media, others have begun with diarrhœa, both of which diseases may be associated with blood-poisoning. We have ourselves seen Laundry's paralysis originate in an acute gastro-intestinal attack with profuse diarrhœa, undoubtedly due to ptomaine poisoning, the poison in this instance apparently paralysing, like urari, the motor end organs. Megrim, again, is a disease which is almost certainly toxically induced, and it is noteworthy that one of the cases of myasthenia gravis occurred in a megrimous patient immediately after an attack of megrim.

It is now fairly well established that tabes dorsalis is a toxic disease, the poison acting chiefly upon the sensory periphery, but also to some extent upon the lower motor neurons, causing the Argyll-Robertson phenomenon, paresis of the extrinsic ocular muscles, and the levators palpebrarum. Now, in the case of the latter muscles, the paresis is often transient; moreover, we have observed the fatigue phenomenon in these cases. Seeing then that transient paralysis and the fatigue phenomenon may be brought about by a toxin, it does not seem improbable that myasthenia gravis may be similarly induced. Assuming the disease to be produced by a toxin, we have to inquire whether the poison is endogenous or exogenous. We know that substances normally present in the body may cause fatigue, and conceivably myasthenia may be due to an excess of such poisons —poisons, namely, produced by the metabolism of the organism. The occurrence of the disease after such maladies as influenza, scarlatina, typhoid, and sore-throat suggests a microbic origin.

The poison may conceivably act upon the motor nervous system, or upon the muscles themselves. In the former case it might involve the upper or the lower neuron or both.

Several arguments may be adduced against the upper neuron being the essential seat of the lesion. The myasthenic reaction and the exhaustibility of the knee-jerks, as met with in Collins' case, the occasional atrophy and diminished faradic excitability, cannot be explained on the assumption of an upper neuron-lesion alone. Nor can we in this way explain the tendency to spontaneous attacks of dyspnœa, attacks so severe as to frequently prove fatal. Nor, again, the tendency to choking from pharyngeal paralysis, seeing that the choking is essentially due to defect of the voluntary part of the act of deglutition. Further, the attacks of palpitation are in no way suggestive of a lesion in the upper motor level. One cannot, indeed, fail to detect a likeness between the attacks of dyspnœa, choking, and palpitation met with in myasthenia gravis, and similar attacks occurring in affections of the lower motor level, to wit, bulbar paralysis and peripheral neuritis—the diphtheritic form, for instance.

But perhaps the most conclusive evidence against the view that the essential lesion is situated in the upper motor neuron is afforded by the myasthenic reaction; the muscles in myasthenia gravis become unduly exhausted by faradic stimulation, the same fatigue being experienced as occurs after voluntary action in this disease. It is evident that this phenomenon must be due to a peripheral cause.

We have next to consider whether the disease involves the lower motor neurons or the muscles. On the assumption that it is of toxic origin, it seems safe to exclude the muscles from an essential share in the pathological process. We have no facts in pathology suggesting that a poison can exist in the blood in sufficient quantity to seriously impair the functional activity of the entire muscle system, and this without producing any other symptoms, much less that such a poison can pick out symmetrical muscles, *e.g.*, the levators palpebrarum, to the exclusion of all others. What we know of the action of drugs and toxins strongly suggests that if myasthenia gravis is due to a *poison*, acting selectively, it produces its effects by acting upon nerve rather than upon muscle.

The myasthenic reaction, while it does not enable us with certainty to fix the lesion upon nerve rather than upon muscle, yet lends support to the view that the former is involved. On this assumption the motor-fibre, end-plate, or muscle-fibre may be implicated. The characteristic reaction is obtained by faradism, not galvanism. Now faradism causes contraction essentially through the nerves; its power of causing contraction by direct stimulation of the muscles is small. The inability of galvanism to cause the exhaustion does not help us, since it contracts the muscles both through the nervous system and by direct muscle stimulation; this inability is doubtless due to the fact that it cannot induce tetanus. The crucial test would be to find if, after inducing complete myasthenia by faradism, the myasthenic muscles respond to galvanism. Such response would afford fairly conclusive evidence that the exhaustion was one of the motor nerve-fibres or end organs.[1]

We have then arrived thus far: the motor end-fibres or end-plates are especially involved in myasthenia gravis. Is the body of the neuron also involved? We can conceive of the toxine acting upon the whole of the lower motor neuron, cell-body, axon, and end-plate. It is indeed possible that it may act primarily upon the cell-body, the axon being secondarily affected through withdrawal of the normal trophic influence emanating from the cell-body. The muscle-atrophy and diminished faradic excitability which sometimes occur prove that the lower motor neuron is, at least occasionally, involved.

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[1] We have, at present, no marked case of myasthenia gravis under observation upon which to make this observation. On the suggestion of one of us (H. C.), Dr. Farquhar Buzzard kindly undertook the following experiment:—In a well-marked case of myasthenia gravis a moderate galvanic current was applied to the biceps muscle and a contraction obtained. The muscle was then faradised until it gave no response to a strong stimulus. Then it was tired out by making the patient flex the elbow against resistance, exerted until all power of flexion was lost. On applying the same strength of galvanic current as used at first an excellent contraction was obtained. Finally, on again applying the faradic current, the muscle was found to be still irresponsive.

The fact that discoverable lesions are generally absent *post mortem* is just what we should expect from the symptoms of the disease. Were a permanent organic lesion present we should not expect such marked variations in the degree of paresis to occur as characterise the disease—complete ability to move the muscles one moment, absolute paralysis of them a few moments later, or an entire disappearance of the symptoms for weeks, months, or years together.

What we know of the action of drugs entirely supports the view that function may be profoundly modified by the action of chemical substances, without any discoverable organic change being wrought. Nothing is more certain than that antagonistic poisons may set up a countless variety of transient perturbations in the nervous system. Witness, *e.g.*, the nervous phenomena observed in dyspepsia, and among these it may be observed that lassitude and muscular fatigue are not infrequent.

But while numerous nervous symptoms may result from blood-poisoning independently of discernible organic lesion, it is a fact that in all cases hitherto known to us of paralysis thus resulting, a well-marked lesion is discovered *post mortem*; we allude to such diseases as peripheral neuritis and poliomyelitis. And herein lies the pathological interest of myasthenia gravis. In it we have, we would suggest, an instance of a toxic paralysis, lasting intermittently for a long period of time, and often terminating in death, and in which, nevertheless, no discoverable lesion is necessarily induced. The wonder is not that such cases are rare, but that they are not more frequent. Purely functional nervous symptoms of toxic origin, such as numbness, tingling, twitching, drowsiness, coma, are common enough; why should not purely functional toxic paresis be equally common? As a matter of fact, we believe that such pareses are not altogether uncommon in a very mild form, more especially in connection with dyspeptic toxæmia.

What we suggest, then, is this—that in myasthenia gravis, a toxin, probably of microbic origin, circulates in the blood, and acts selectively upon the lower motor neuron, so as to modify its functional activity. This change in functional activity is such that the lower neuron soon becomes exhausted by the transmission down it of stimuli, whether originating in an act of will or started by the faradic current. As to which part of the neuron the poison acts primarily upon one can only vaguely surmise; but we lean to the view that it is upon the axon. This brings the disease into line with such a disorder as diphtheritic neuritis. Imagine an attenuated toxin, such as causes this latter disorder, to remain for some time in the body, and the effect might be much the same as is observed in myasthenia gravis. In the earlier stages of the disease no organic changes would be produced, but after prolonged action one might expect such changes to occur, and be accompanied by atrophy of the muscles and diminished faradic excitability.

DIAGNOSIS.

The diagnosis in well-marked cases of myasthenia is easy. The paresis and speedy fatigue of voluntary muscles on exertion, the myasthenic reaction, the absence of muscular atrophy and of fibrillary tremors, of objective sensory disturbance, trophic changes and sphincter affection, together with the remarkable variations in the intensity of the symptoms—form a distinct clinical picture.

A diagnosis can often be made at first glance from the facial expression, the ptosis, and nasal speech.

The diseases most liable to be confounded with myasthenia gravis are hysteria, bulbar palsy, polioencephalitis, the muscular distrophies, amyotrophic lateral sclerosis and general asthenia.

No doubt in hysteria and neurasthenia ready fatigue after exertion is met with, while the variations in the symptoms, the presence of ptosis, difficulty in swallowing, and attacks of breathlessness, all occur. In such cases absence of a nervous heredity and hysterical manifestations, the absence of sensory symptoms and the presence of the myasthenic reaction, should enable a diagnosis to be arrived at.

Cases undoubtedly occur in which the diagnosis is very difficult.

A case recently seen by one of us illustrates the difficulty which may arise in diagnosing early cases. The patient was a young married woman, who for three years (since her last confinement) had suffered from general muscular weakness. When first seen, after ascending a long flight of stairs, she was much exhausted and very breathless, speech was somewhat nasal in character, and she had slight double ptosis. She complained of general exhaustion after any slight exertion, had had definite diplopia on several occasions, and said she had been very anæmic ever since her confinement. No weakness in the jaws or trouble with deglutition existed, and although the symptoms were very suggestive the facts did not justify a certain diagnosis, especially in the presence of a marked anæmia.

In the myopathies fatigue after exertion is often complained of. We have already seen that the facial appearance is very similar to that seen in the Landouzy-Dejerine form of myopathy. The waddling gait and the tendency for the paresis to affect the proximal muscles of the extremities are other points of similarity; but, as Oppenheim (58) remarks, the resemblance is superficial only, for it is only in myopathic patients, who show the fatigue phenomenon, and those in whom the muscles are only slightly wasted, that any confusion is likely to arise (Jolly, 58). Toby Cohn (58) argues from Laquer's case, in which muscular atrophy developed, that the relation to the myopathies is closer than would appear at first sight.

Wernicke's case (16) was diagnosed at first as one of amyotrophic lateral sclerosis with bulbar symptoms, the absence of muscular atrophy being specially remarked upon.

From bulbar palsy the disease distinguishes itself by the presence of ptosis, upper facial weakness, paresis of the jaw and neck muscles and of the extremities, and by the myasthenic reaction. The variation in intensity of the symptoms is a diagnostic point of great importance.

Lastly, the differentiation from polioencephalitis has to be considered. Here the diagnosis may be extremely difficult. The mode of onset, absence of muscular wasting, and above all the variability of the symptoms, are points to which especial attention must be directed.

PROGNOSIS.

Of sixty recorded cases twenty-three ended fatally.

The average duration of life of the fatal cases was about a year and a half after the development of the first symptoms.

These figures probably give an exaggerated impression as to the fatality of the disease.

In one case, that of Widal and Marinesco (33), death occurred fourteen days after the first symptoms were manifested. In Dreschfeld's case (14) the patient lived fifteen years.

That cases improve in a remarkable way and remain free from symptoms for months, or even years, is certain. That complete recovery sometimes takes place is probable. Goldflam (9) described his cases as belonging to "a curable form of bulbar paralysis." In one of Erb's cases (2) the patient was in good health four years after his symptoms had disappeared. In some cases the disease lasts a number of years.

Involvement of the respiratory muscles, with consequent attacks of dyspnœa, is a symptom of the gravest significance, and the patient's friends should be warned that death may occur suddenly during one of these attacks.

Any pulmonary disorder, whether chronic or acute, is to be considered as of very serious import.

TREATMENT.

No specific treatment is known for the disease. The patient must be enjoined to take as much rest as possible, and in severe cases should be confined to bed.

Excitement of every sort is to be avoided, inasmuch as the symptoms are much increased by it.

Since cold appears, in some cases at least, to aggravate the disease, attention should be paid to the patient's clothing. Cold baths are to be avoided. The patient's whole life is to be regulated so as to avoid muscular fatigue.

The diet should be nutritious, and if there is any difficulty either in deglutition or mastication, the food is to be carefully chopped, to obviate the necessity for chewing, and to avoid, as far as possible, the risk of choking.

In the event of the necessity arising for using the stomach tube, the greatest care must be taken, for, as in other forms of bulbar palsy, the procedure is not unattended with risk; indeed, in a case reported by Oppenheim, a fatal result followed the passage of the tube.

As to drugs, little can be said. Erb and Goldflam's cases were treated with iodide of potassium and mercury, but there is no evidence to show that this treatment actually has a beneficial effect.

Strychnine was employed by Strümpell (24) in large doses without result. In Buzzard's cases hypodermic injections of strychnine up to one-sixth of a grain in the twenty-four hours were given without benefit.

Faradism, galvanism, and massage were all given an extended trial in Buzzard's male case. Faradism appeared to do harm, the patient feeling weaker as the result of the treatment, while galvanism and massage did no good. Galvanism to the spine has been recommended by Erb (2) and Goldflam (13), but appeared to have no positive value in the case already referred to.

Suprarenal extract was also ineffectual. Under thyroid tabloids, together with a daily injection of five minims of solution of strychnine, the patient improved so much that after six weeks he felt almost well. The improvement began on the day the thyroid was commenced, but it is quite possible that suggestion may have accounted for the success which attended this line of treatment; the case relapsed while still taking the tabloids.

In another case thyroid extract was given without benefit.

Iron and arsenic appear to be of use as general tonics, although they have no specific action upon the disease.

NOTES OF SIXTY REPORTED CASES OF MYASTHENIA GRAVIS.

Case 1, Wilks (1).—A stout girl, looking well, came to the hospital on account of general weakness; she could scarcely walk or move about, she spoke slowly and had slight strabismus. She remained in this state about a month, being neither better nor worse; every movement of her limbs and her speech were performed so slowly and deliberately that the case seemed rather one of lethargy from want of will than an actual paralysis.

At the end of this period the symptoms became aggravated, and in about three days they had assumed all the well-marked characters of bulbar paralysis. She spoke most indistinctly, swallowed with great difficulty, and was quite unable to cough. The limbs were, however, not paralysed, she was able to get out of bed. It was shortly afterwards seen that her respiration was becoming affected, the difficulty of which rapidly increased and in a few hours she died.

The medulla oblongata was very carefully examined and no disease was found. It appeared quite healthy to the naked eye, and the microscope discovered nothing abnormal.

Case 2, Erb (2).—Man, aged 55. Illness developed slowly with pains in the nape of the neck; after four months he could not hold his head up; the muscles of mastication were weak, and he had double ptosis. Thereupon ensued weakness in the tongue and difficulty in swallowing; the mouth was kept open. There was atrophy of the neck muscles and trapezii, and slight diminution in the response to faradism in the trapezii, masseters and splenii. There was a high degree of auditory hyperæsthesia on the left side. Decided improvement occurred after a six months' course of galvanism. He could hold his head up, swallow well, and masticate much better. After a few months he became well, though he still had occasional weakness in the arms.

Case 3, Erb (2).—A peasant woman, aged 30, was seen on October 30, 1870. For nine weeks she had had slight twitchings in the face, diplopia and ptosis; later, difficulty in mastication, stiffness in jaws, much headache and giddiness developed; recently, she has suffered from palpitation and weakness in the limbs. She has had blinking of the eyes and twitchings about the mouth for a month.

State.—The eyes are half closed, the movements of the eyeballs are very defective, there is no diplopia, she has difficulty in opening and closing the mouth, the mouth is constantly open, and there is some stiffness and weakness of the facial muscles. A feeling of weakness exists without actual loss of power in the lower extremities. She has some left auditory hyperæsthesia.

November 4.—The symptoms are worse. She complains of difficulty in swallowing, and of a profuse salivary flow.

November 10.—There is improvement in the eye muscles and muscles of mastication. She says that for many weeks the head has felt heavy and she has had difficulty in holding it up, while there has been a feeling of weakness in the posterior cervical muscles.

December 22.—Great improvement.

January 17, 1891.—She is slightly worse. The tongue appears atrophied. During the next month fluctuations in the severity of the symptoms occurred.

July, 1891.—Is much worse again. She now has ptosis, diplopia, difficulty in mastication, and atrophy of the masseters. The movements of the soft palate are sluggish; speech is nasal; utterance difficult; the voice is weak, especially after lengthy speech. There are great weakness and fatigue in the legs; she has frequent palpitation. Pulse 100.

Improvement again occurred, but later she became worse and died suddenly on the night of April 24, the illness having lasted eight months. There was no *post mortem*.

Case 4, Erb (2).—A merchant, aged 47, was seen on July 11, 1871. During the last year he had suffered from pain in the occiput, and stiffness and weakness in nape of neck. Since April last he has had sharp pains in head and nape of neck, vertigo and occasional dimness of vision. Towards the end of May weakness in the arms and legs compelled him to remain in bed; he could with difficulty hold his head up. In June he developed double ptosis and was very sleepless; during the last few weeks has been better.

Present condition.—A powerful man. He has slight paralysis of the upper face, he cannot wrinkle the forehead well and there is slight twitching of frontalis. The head is bent forward. The right side of the palate is weak; swallowing is unaffected, but there is occasional fatigue of masticatory muscles. Walking soon causes fatigue, while vertigo and dimness of vision occur after walking much.

No improvement followed fourteen applications of galvanism.

Case 5, Erb (2).—A male, aged 48. His previous health was good. Six months ago the lips felt stiff, and he had headache and diplopia. Three weeks later he had pain in the neck and the head fell forward, later there was difficulty in chewing and swallowing. Pain and weakness in arms and legs, giddiness and ringing in the ears developed. The voice became hoarse and the movements of the tongue difficult, while ptosis developed.

Present condition.—He has difficulty in speaking, chewing and swallowing. The pupils react normally, the extrinsic eye muscles are unaffected. There is weakness in the right arm, and fatigue is easily produced. He has severe pains in both arms and legs at times. Fibrillary twitchings are seen in the tongue, which is slightly atrophied.

The patient went out of the Klinik much improved after fifty-two applications of the galvanic current.

Case 6, Eisenlohr (4).—A girl, aged 18. *As a child she had suffered from megrim.* This was *occasionally accompanied by ptosis. Two years ago she developed sudden diplopia,* which disappeared after a three months' course of iodide, but returned in the summer of 1885; sometimes chiefly on one side, sometimes on the other. In July, 1886, after an attack of megrim, she had weakness of both hands. In August there developed slight weakness of the legs, breathlessness on quick movement, and difficulty in swallowing, chiefly at midday and in the evening, also weakness of cervical and masticatory muscles. All these symptoms varied in severity even in the space of a single day.

August 16.—The patient was examined. She has ptosis, chiefly left-sided, with little movement of the eyes; can only close the eyes feebly; there is double facial weakness and little movement of the soft palate; she can only swallow small quantities of fluids, which readily regurgitate through the nose; she has great difficulty in moving the head; the respiratory movements are defective and the cough is weak; there is paralysis of all four extremities; swallowing is easy in the morning, difficult in the evening, and movements of tongue are fatiguing. Respiration is superficial; pulse frequent.

August 18.—Palpitation; pulse 140; frequent respirations with fruitless efforts to expectorate accumulation of mucus, &c., from the throat.

August 21.—The diaphragm is almost entirely paralysed. Death.

Post mortem.—The cortex cerebri was not examined. Hyperæmia with small recent *ante-mortem* extravasations was found in the medulla, numerous small but not degenerated fibres (fasern) in the roots of the hypoglossal vagus and accessorius were observed.

Case 7, Oppenheim (5).—A maidservant, aged 29, seen February, 1885. *Nine months ago she noticed weakness in the hands*, which gradually increased and involved the legs also. For the last four weeks she has noticed fatigue during speaking and has often to pause, also weakness of lips and difficulty in swallowing.

Present condition.—There is little movement of the facial muscles during speech; voluntary movement of the lower face is very defective; there is weakness in opening and closing the jaws; mastication rapidly causes fatigue; she cannot move the lower jaw laterally; there is defective movement of the soft palate during phonation; there is tremor of the tongue with defective movement; speech is nasal. She cannot cry out; inspiratory movements are defective; she complains of breathlessness; there is great weakness in arms and in the abdominal muscles; she says that the degree of weakness in the extremities varies greatly from time to time. Sight is normal. There is no muscular atrophy, no electrical change, but the deltoid and biceps require unusually strong currents to excite contraction.

June, 1885.—Manifest dyspnœa. In the following month attacks of difficulty in swallowing and speaking developed.

August, 1885.—She has weakness in the orbicularis palpebrarum, and attacks of dyspnœa; the paralysis is increasing with slight remissions.

January, 1886.—She complains of pains in nape of neck, occasionally in the extremities and face.

May, 1886.—There is increased weakness in extremities, she can scarcely hold her head up.

September, 1886.—She died in a dyspnœic attack with pneumonia.

Case 8, Lauriston E. Shaw (6).—A baker, aged 37. He had enjoyed good health until the present illness. Six months ago he had a severe attack of diarrhœa lasting a fortnight. Ever since then he had had a feeling of weakness, especially in the muscles of mastication, the arms, and to a less extent, in the legs. After this difficulty in articulation and swallowing supervened. The weakness was slight in the morning and increased as the day advanced. He has had two attacks of dyspnœa within the last fortnight; there has been a copious secretion of frothy mucus with difficulty of expectoration.

Admitted, February 12, 1887.—He can barely stand; he says he often falls down. The soft palate is normal. The mouth is constantly held slightly open. There is loss of power in the lower facial muscles. The naso-labial fold is obliterated, causing a vacant expression. There is some difficulty in protruding tongue; the masseters are weak; he cannot hold a pipe either with the lips or teeth; has difficulty in swallowing and occasional diplopia; the tendon reflexes are brisk; spurious ankle clonus is present on the right side; the cremasteric and plantar reflexes are normal, the abdominal and epigastric absent. The mental condition is good; he has perfect control over the bladder and rectum.

He died shortly after admission from dyspnœa, apparently resulting from paralysis of the muscles of respiration.

Post mortem.—Pons, medulla, and cord were examined by Dr. Newton Pitt, and nothing abnormal discovered.

Case 9, Bernhardt (7).—A joiner, aged 44. In August, 1886, he first complained of fatigue and weakness in the eyes, later he had diplopia.

Present condition.—November, 1886. There is double ptosis, on the right side chiefly; the left external rectus is paralysed. After chewing for a short time he cannot close jaws. Under potassium iodide and galvanism he was dismissed cured in February, 1887, and continued well till 1890.

July, 1890.—The head falls forward on chest, chewing and swallowing are difficult, and speech soon becomes nasal; the lips are fatigued after continued speech, and work easily exhausts him. Movements of the arms are difficult; there is slight right ptosis; the electrical reactions are normal, but there is slight quantitative diminution in the neck muscles.

September, 1890.—He has dyspnœa on walking quickly, or on mounting steps. *The right vocal cord moves less readily than the left.* He improved under potassium iodide and electrical treatment.

1890.—Sudden death occurred. No *post mortem* was allowed.

Case 10, Jolly (8).—A tanner's apprentice, aged 15, was admitted on August 19, 1890. The family history was unimportant. He had suffered from middle ear disease for a few years, and had had no other illness of importance. His present trouble began eight months ago with weakness in the legs; later, weakness in the arms, difficulty in speaking, giddiness, and pain in the neck and sacrum developed. After walking a short distance he requires support to prevent him falling. He has double ptosis; fatigue soon develops after whistling, speaking, chewing, or swallowing; the eye movements are good. The knee-jerks are somewhat increased. There are no qualitative electrical changes, but the quantitative estimation is peculiar, the muscles at first respond well, but if the same muscle is stimulated repeatedly so that a tetanic contraction is produced, the contraction of the muscle gradually becomes weaker until it is only elicited by very strong currents—in other words, the reaction of fatigue is present.

The patient died suddenly on March 18 while eating, a piece of food sticking in his throat. At the autopsy nothing abnormal was found either in the nervous system or muscles.

Case 11, Jolly (8).—A boy, aged 14, who had been strong and healthy until the summer of 1893. At that time (one and a half years ago), while at school he noticed that he could not see the black-board properly, for he was unable to keep his eyes open, the eyelids drooping if he looked at an object for any length of time. After a rest, and particularly in the morning, this was not the case. Later, tiredness of the legs, also of the arms, of the neck and lip muscles, appeared. While eating he had to stop frequently because he could not go on chewing. If he read aloud, speech became indistinct, reminding one of general paralysis; there was no affection of the tongue or of swallowing. All voluntary muscle was readily exhausted, and also the exhaustion of one group of muscles was seen to produce fatigue in others; if, for example, the legs are tired, then the arms become fatigued, though not to the same degree.

Case 12, Senator (10). (*Doubtful case.*)—A workman, aged 41. Twenty years previously he had an ulcer on the penis and swelling of glands; no other evidence pointing to syphilis. Been feverish for nine weeks and had a slight cough, rigors, heats, sweats, and nasal speech. On the night of November 27 and 28 he had difficulty in swallowing and speaking, tongue was immobile, and there was little power of moving the jaws, a fixed expression, and the eyes seemed large. November 29 he could not move his right arm, there was a tendency to walk to the left and he drags the right leg.

Present condition.—He cannot speak; pulse 64; respiration 28. He can only move the right arm slightly; the right leg is paralytic; the plantar and patellar reflexes are active; rather more on the right side. There is paralysis of all the muscles supplied by the facial nuclei; laughing and whistling are impossible. He cannot close his eyes properly. He keeps the mouth half open and cannot powerfully close it. The lateral movements of the jaw are unaffected; the tongue is motionless; he has great difficulty in swallowing; the electrical reactions are normal, but the left facial muscles require a stronger current than the right. Involuntary twitchings of the mouth occur; there is diminished movement of the soft palate; the eyeballs are prominent.

The condition gradually improved with slight fluctuations till February, 1885, when he got worse. Death occurred from exhaustion in March, four months after beginning.

Post mortem.—A microscopical examination of the base of the brain, cord, peripheric nerves and muscles, revealed nothing morbid.

Case 13, Senator (10). (*Doubtful case.*)—A woman, aged 36. She is very anæmic and is suffering from sarcomata of the ribs. She developed in the course of the illness a nervous affection, pains in the head, back, and lower extremities, together with a feeling of fatigue. At this time albumosuria was first detected. She complained of difficulty in swallowing; she said that her chin felt as if it were dead and "did not belong to her." It was found to be quite anæsthetic. The tongue was almost completely paralysed; it was not atrophied, though fibrillary twitchings often seemed to occur about the middle of the tongue. The pulse rate was increased. The electrical reactions in the face and lower limbs were normal; in the tongue excitability was diminished. Death occurred somewhat suddenly.

At the *post mortem* multiple sarcomata of the ribs, double fibrinous pleurisy and chronic parenchymatous kidneys with waxy change; neither in the brain nor medulla was anything found to account for the condition.

The severe anæmia, Senator thinks, may have produced the symptoms by acting upon an imperfectly developed nervous system. Senator remarks that nervous symptoms have been present in several cases of multiple myeloma, *e.g.*, in Stockvis's case there was defective speech and swallowing, together with salivation, paralysis of the facial and trigeminus nerves, and paraplegia.

Case 14, Hoppe (11).—A blacksmith, aged 40, family history good, no syphilis. The illness began by double ptosis, followed by weakness of the muscles of mastication, and difficulty of speech and swallowing. Examination showed paralysis of the right internal rectus and left superior rectus, the upper and lower part of the facial; great weakness of the masticatory muscles; little movement of the soft palate, paralysis of adductors and abductors of vocal cords; great weakness of the extremities.

The electrical reactions were normal, and there was no muscle atrophy.

The patient died, and no pathological lesion was found *post mortem.*

Case 15, Remak (12).—A girl, aged 12. She had influenza in February, 1890, with suppuration of the left ear. In July it was noticed that the eyes did not close during sleep, and speech was often indistinct. In September she complained of difficulty of swallowing. She had a fixed facial expression, the tongue was weak and the soft palate sluggish. Speech was nasal and indistinct, and after speaking a little while she could not articulate at all because of weakness in the tongue and lips. The difficulty in speech and swallowing improved under galvanic treatment. She had difficulty in getting up expectoration, and often dyspnœa.

October 6.—There is slight tremor of tongue, she cannot raise the tip.

October 16.—She has slight weakness of the arms.

October 21.—Pulse 120. Severe dyspnœa in consequence of weakness of the respiratory muscles; swallowing is impossible.

November 5.—Intense dyspnœa; death. No *post mortem.*

Case 16, Goldflam (13).—A male, aged 25, house-servant, was seen on December 22, 1891. His illness began suddenly seven weeks ago, with headache, giddiness and limitation of the movements of the head. A week later disturbance of speech and swallowing set in, followed by weakness in the arms—a few days later in the legs. Recently he has had severe pains in the shoulder and sacrum. There is no history of syphilis or alcohol.

Present state.—A fairly well-developed man; his speech is nasal. There is very little mobility of the soft palate; the pharyngeal and laryngeal reflexes are markedly diminished; swallowing is difficult; fluids frequently regurgitate through the nose; mastication is fatiguing. The lateral movements of the lower jaw are feeble, he cannot open the mouth widely; the tongue movements are good; lagophthalmos is present, greater on the right side; the conjunctival reflexes are diminished; the pupils react well; the neck muscles, sterno-mastoids, and trapezii are weak.

The patient cannot lift his hands up to the horizontal. The respiratory excursions are feeble. He does not complain of dyspnœa. The legs are feeble. The deep reflexes increased. There is no ankle clonus and no atrophy or fibrillary twitchings, while the electrical excitability of the muscles is normal. There is no affection of bladder, rectum or sensation.

January 9, 1892.—The abdominal muscles are feeble. The knee-jerks are poor and more difficult to elicit the longer one tries.

January 25.—The patient feels weakest after sleep, after a few movements he is better. In blowing the nose air comes through the mouth.

February 8.—The knee-jerks become feebler the longer the tendon is struck, that on the right side finally disappearing.

February 10.—It is especially the large muscles near the trunk which are affected. Tiring of the extremities diminishes the power in the others.

January 4, 1893.—He remains now practically well.

Treatment.—Galvanic stream to the spinal cord. Potassium iodide, iron and arsenic internally.

Case 17, Goldflam (13).—A male, aged 25, was seen in April, 1892. Ten years ago he had typhoid, which lasted three months. A mental affection followed. He refused to take food, was morbidly shy and tried to commit suicide. The present illness began four months ago, without observable cause, with weakness in the arms and legs. These symptoms developed in the course of two weeks. Shortly after he had difficulty in chewing. The neck muscles became affected, and giddiness developed. A month ago he had a very bad attack of dyspnœa and general loss of power of movement.

State.—A well-developed man. There is paresis of the lower face; he cannot whistle. He can shut the eyes well; the tongue and palate act normally. Chewing is difficult. There are no psychical disturbances; patient is, however, anxious about his condition. The neck muscles are feeble; the deltoid and upper arm muscles are most affected, while in the lower extremities the flexors and extensors of the hip are chiefly involved. The tiring of one extremity appears to have no influence upon the others. The deep reflexes are increased; there is slight ankle-clonus. The muscles all react normally to electricity. The symptoms vary from day to day.

July 1.—The deep reflexes are somewhat difficult to obtain.

March 16, 1893.—The patient is now almost well. He has had two relapses, both brought on by a fright.

May, 1894.—The patient only remained well for six months; the symptoms are again present.

Case 18, Goldflam (13).—Governess, aged 22, was seen on April 13, 1892. With the exception of anæmia and headache, especially during the last winter, she has always been healthy. The present trouble began three weeks ago without discoverable cause, with headache, photophobia, trembling in the eyelids, and diplopia. A week later she had a feeling of oppression, then of weakness and heaviness in arms and legs; later still, right-sided ptosis and difficulty in chewing, the jaw tended to fall down and had to be supported by the hand. Fluids came through the nose. The voice became nasal. There were no signs of hysteria. The patient's father died of a brain tumour; her mother had a congenital divergent strabismus.

State.—A fairly well-developed, rather pale girl; internal organs normal; pulse 90. Except for the right-sided ptosis, the eyes are normal. There is lower facial weakness and paresis of the palate, its reflex excitability being diminished. The tongue is somewhat thin, but its mobility is normal. Speech nasal, and chewing difficult. The movements of the head are weak. The head tends to fall forward. The deltoid appears to be the weakest muscle of the arms. There is very little weakness in the lower extremities. The electrical excitability of the muscles is normal. The deep reflexes are very active. She suffers from attacks of dyspnœa.

May 2.—Swallowing is difficult.

September 20.—She is much better; the nasal voice is still present, but no other symptoms of the disease.

Case 19, Dreschfeld (14).—A widow, aged 36. Fifteen years ago she developed sudden double ptosis, but completely recovered in six months. Ten years ago she had a second attack of ptosis with diplopia, followed by difficulty in speaking and swallowing, and weakness in the arms; she had to stop eating frequently because her jaws ached; she could not properly open her mouth to protrude the tongue, and she lost the power of whistling. The eye symptoms improved, but about nine months afterwards she suddenly became worse and was admitted.

On admission.—The intrinsic ocular muscles are normal; she has ptosis, and the extrinsic muscles supplied by third nerves are nearly completely paralysed; while the fourth and sixth on both sides are completely paralysed; the masseters, pterygoids and temporals are much weakened; she cannot close the eyes, wrinkle the forehead, or frown, press the lips together, smile or whistle.

The movements of the tongue are very limited, it is somewhat atrophied; the depressors of the hyoid are weak; the soft palate is paralysed, there is no palatal reflex; there is difficulty of swallowing; great difficulty in clearing fauces and posterior nares of saliva and mucus. Difficulty in articulation; the laryngeal abductors are weak; the sterno-mastoids and trapezii are somewhat atrophied; the diaphragm acts slightly; the deltoids are atrophied and paralysed; there are no fibrillary twitchings; pulse 130; the wrist and triceps reflexes are markedly increased. The facial muscles show no reaction of degeneration.

November 22.—The patient is much worse; she is markedly cyanosed, the respirations are spasmodic and dyspnœa is great; swallowing is impossible, and there is no longer true articulation; the patient can only produce a faint grunt. The pulse is at times intermittent, weak and thread-like. During the night the breathing became much more laboured, the temperature rose to 99·5, and the patient gradually sank and died.

Post mortem.—Careful microscopic examination revealed nothing. The muscles were not microscopically examined.

Case 20, Suckling (15).—A barmaid, aged 21, complained of great general weakness. A brother has epilepsy, a sister paralysis. The patient's illness commenced three years ago with weakness in the arms and later in the legs. She attributes her illness to overwork. Eighteen months ago, while singing, her tongue became paralysed and she could not articulate distinctly. Twelve months ago she had difficulty in swallowing and liquids came down her nose. Five months ago she began to have suffocative attacks. There is no history of diphtheria.

State.—There is slight double ptosis, the eye movements are sluggish and restricted in all directions, especially upwards. The right eye cannot be turned up at all and forced movements in any direction are attended with nystagmus; diplopia is present at times, the pupils and discs are normal. She could not close her eyes tightly and fibrillary tremor of the ocularis muscle occurred when she tried to do so. The tongue is weak, and speech indistinct. There is difficulty in swallowing; no paralysis of the soft palate could be discovered. The palatal reflex is present; mastication is impaired. The arms cannot be lifted from the shoulders, the deltoids are large and all the other muscles normally developed; there are no sensory changes, no exaggeration of the reflexes and no electrical changes. The spinal muscles are weak, she is unable to sit up; when lying down she cannot get up at all without assistance; the legs are very weak, she cannot lift them off the bed. The gait is slightly waddling, and she would fall if not supported. The knee-jerks are a little increased, no ankle clonus, plantars absent. There are no sensory changes. The feet and hands are blue. The patient cannot lie down in bed, as she dreads an attack of suffocation. An attempt to examine the throat brings on inspiratory stridor and cyanosis to such an extent that the patient seems to suffocate. There are no hysterical symptoms. She remained under observation three months, when she was *in statu quo*.

Case 21, Suckling (15).—A female, aged 18, with a neurotic family history. Her illness is attributed to exhaustion, and commenced gradually three years ago. She is unable to walk more than a hundred yards without becoming exhausted. The arms are weak and the grasp feeble. She cannot hold her arms out or place them on her head. There is slight ptosis, squinting, and diplopia at times. The movements of the eyeballs are restricted in all directions. Nystagmus is present. The knee reflexes are a little increased, there is no ankle clonus. There are no electrical changes. She complains of difficulty in swallowing and mastication. After mastication the jaw drops, she has difficulty in articulation. She is slightly choreic, has no suffocative attacks, and there are no hysterical symptoms.

Case 22, Wernicke (16).—A female, aged 16, admitted June 16, 1893, with the following symptoms: Ophthalmoplegia externa, incomplete double ptosis, bilateral facial weakness, upper and lower. Paresis of motor fifth and of muscles of deglutition; only fluids can be swallowed and they occasionally come through the nose. No affection of the tongue or speech. Paresis to a marked degree of both neck and shoulder muscles. Upper arm, forearm and hand weak, but she can use them still. Thigh muscles slightly stiff, otherwise the legs are not affected. Her illness developed gradually four months ago with slight temporal headache. The electrical excitability of the muscles is intact although in a few muscles quantitatively slightly diminished. The tetanic induction stream produces instead of a lasting only a temporary muscular contraction. The doubtful diagnosis was amyotrophic lateral sclerosis with bulbar complications.

July 17, 1893.—She was admitted to Clinik of Professor

Mendel. She now has palate, tongue and jaw weakness, and anæsthesia of the pharynx and larynx.

Sixteen days after admission the patient died suddenly of asphyxia. The autopsy was negative; the only change being considerable vascular dilatation, particularly in the Hirnstan, and numerous recent hæmorrhages.

Case 23, Mayer (18).—A patient suffering from difficulty in speaking and swallowing, weakness of the jaws, bilateral ptosis, paresis of extremities, and abnormal fatigability; the symptoms were worse towards evening and after exertion. There was no atrophy and no disturbance of the reflexes. Temporary improvement was followed by sudden death by choking.

Post mortem.—It was found that the cells of the hypoglossal nucleus, with the exception of a small number which were vascuolated, were completely normal, as were the cells of the anterior horns and pyramidal tracts. On the contrary, there was a marked pathological change in the intra-medullary portion of the anterior roots, also in the hypoglossal root, particularly distinctly seen in Marchi preparations, such preparations showing all along the anterior roots, as also in places on the hypoglossal root, stripes and flakes of dark myelin. The intra-medullary parts of the anterior roots, as well as of the hypoglossal root, appear distinctly atrophic, when the nerve sheath stain (Markscheiden färbung) is used.

Case 24, Strümpell (24).—A female, a field-worker by occupation, aged 21. Admitted December 30, 1893. Ten months ago she began to have difficulty in speaking and in raising the upper eyelids; six months ago she noticed weakness in the arms after working in the fields, and in the legs after walking, also difficulty in swallowing and chewing, and double vision.

Present state.—There are bilateral ptosis, weakness of the face and jaw muscles, and weakness of the extremities without atrophy. Speech is indistinct, the letters *b, d, g, j, m, n, s*, are especially badly pronounced. Sensation and the sphincters are normal; the reflexes are normal and could not be exhausted, although after repeated tapping the knee-jerks seem to diminish slightly in activity, great exhaustion is rapidly produced and amounts to almost complete paralysis of nearly all the muscles. She was worse at the menstrual periods. From January, 1894, until she died she had almost daily severe attacks, during which, if walking, she would fall suddenly to the ground, become cyanosed and breathless. Respiration became noisy, sputum accumulated in the mouth, she could neither spit it out nor swallow it; the tongue sank back; if in bed she would sit up with her head bent forwards, saliva flowing out of the mouth. The arms when raised fell flaccid by her side, the extremities were cold. She developed a catarrhal pneumonia, and died suddenly during one of these attacks.

A *post mortem* was made, the medullary nuclei being particularly examined, and no changes were found.

Case 25, Murri (25).—A patient suffering from severe bulbar symptoms, characterised by a tendency to improvement. The disease has lasted for ten years; the myasthenic reaction is present, and the early exhaustion after exercise. In this case, even when complete exhaustion was produced in the muscle by an undue current, the muscle can be readily contracted, voluntarily (and the reverse).

Case 26, Charcot and Marinesco (22).—A boy, aged 13, suffering from complete ophthalmoplegia externa, complete paralysis of the lower, incomplete of the upper, extremities, trunk and face. Death occurred after three months with bulbar phenomena. The symptoms developed in the order above mentioned. There is no affection of sensation nor of the sphincters, and no mental change. There is no affection of the internal organs except an enlargement of the thyroid gland. There are no qualitative electrical changes, but in some muscles there is diminished excitability both to the galvanic and faradic currents.

Post mortem.—Some recent hæmorrhages were found beside the aqueduct of Sylvius, and some others, but less pronounced, at the level of the ventral nucleus of the vagus. No other changes were met with in the central or peripheral nervous systems.

Case 27, Pineles (23).—A male, aged 25. No ætiological factors were discoverable. The onset of the disease was sudden, with headache, giddiness, diplopia, and right-sided ptosis.

In July, 1893, he had difficulty in chewing and swallowing, nasal and indistinct speech, weakness in the arms and legs, and attacks of dyspnœa and palpitation. All these symptoms developed within a few weeks, and were most marked towards evening. The mental state and sensation were normal; there were no hysterical stigmata. There were no electrical changes and no atrophy. The knee-jerks were somewhat active; the palate reflex was present.

Pineles records two other cases which ended fatally after one and a half and two years respectively, death being due in each case to an attack of dyspnœa.

Case 28, Collins (26).—A woman, aged 27, the mother of two healthy children. Three years ago, when six months pregnant, she complained of weakness of the extremities, and soon after left-sided ptosis and diplopia developed, the ptosis disappearing after two or three months. Ptosis of the other eye then appeared, lasting for two months. Following this there developed difficulty in articulating, fatigue on chewing food with difficulty in swallowing and in moving the tongue, with almost complete inability to move the extremities. On first attempting to talk speech is fairly distinct, but soon the tongue becomes heavy, the lips unwieldy, the voice hoarse, weak and nasal. Fluids regurgitate through the nose on swallowing. The weakness is sometimes greatest in the extremities, at others in the muscles supplied by the cranial nerves. The intrinsic muscles of the eye are normal. Attacks of distressing tachycardia and paroxysmal dyspnœa occurred.

These symptoms improved, but she relapsed three months ago. She wakened one morning with paralysis of one side of the face which lasted three days. Since then gradual improvement has occurred. She can now walk provided she does not overtax her strength. She cannot tightly squeeze her eyelids together, she cannot hold her lips firmly together, the tongue is weak (not atrophic), the voice nasal, labials are imperfectly pronounced; the arms easily tire.

The reflexes at first appear normal, but after striking the patellar tendon several times the response gets less and less, finally ceasing to reappear after rest. There is no reaction of degeneration. The electrical responses are normal. There are no fibrillary twitchings.

Case 29, Fajersztajn (27).—A man, aged 23, was seen in April, 1895. He was said to have caught cold ten days previously. This led to great weakness in the legs and difficulty in chewing, swallowing and speaking.

Present condition.—Slight ptosis. The patient tries to prevent this by over-action of the occipito-frontalis. Blinking does not occur often; there is slight lateral nystagmus on looking to the lateral extremes, the orbicularis palpebrarum is weak, especially after frequent closing of the eyes. He can whistle for a few seconds; he can only blow out light two or three times; occasional slight fibrillary twitching of mentalis occurs; the tongue easily gets tired; the pharyngeal reflex present; there is decided weakness of the masticatory muscles increasing with their use. Biting crusts causes great fatigue. There is difficulty in swallowing; the cervical muscles are weak, but the head is held erect. Speech is nasal, weak and rough, and becomes more nasal and weaker when continued; after counting forty to fifty slowly, he becomes aphonic. The breathing is chiefly diaphragmatic and is quickened by the slightest effort; there is decided weakness of the trunk muscles, and he cannot raise himself into the sitting posture while in bed without using his arms; he can only lift his arm over his head ten to fifteen times, even lifting a spoon to his mouth soon tires him; he can write twenty to thirty letters with a steady certain hand, when the writing becomes irregular and soon impossible. There is similar weakness in the lower extremities; he is obliged to rest after walking a few paces. The plantar, cremasteric and abdominal reflexes are normal; the tendon-jerks and electrical reactions are normal.

After six months' rest in bed and administration of strychnine, improvement in all the symptoms followed; afterwards at times there were transient relapses The symptoms were always worst towards the end of the day.

Case 30, Silbermark (28).—A male, a cook, aged 34, entered Nothnagel's Clinik, June, 1896; his family history and previous health were satisfactory. In December, 1894, he found when rolling dough that the third and fourth fingers were weak and tended to drop. After a short improvement, weakness and a feeling of fatigue appeared in the upper limbs, a few months later in the lower. Difficulty in chewing, and regurgitation through the nose appeared, together with facial weakness, difficulty in swallowing and nasal speech. Great variations occurred in the intensity of the symptoms. He always felt better in dry, warm weather than when it was cold and damp.

State.—June 5, 1896. A slight degree of ptosis is present. The ocular movements are free; von Graefe's symptom is present; the pupils react well. There is no weakness of the jaw muscles. The facial weakness is most marked on the left side. There is no weakness of neck; the limbs are affected. Tiring of one hand had no effect on the other.

Case 31, Devie et Roux (29).—An unmarried woman, aged 43, entered hospital July 3, 1894. The symptoms gradually developed two to three months ago without any affection of her general health. She has almost complete paralysis of the extensors and rotators of the head and neck: the head falls forwards, the chin touching the chest; she can only with great difficulty lift the head without using her hands. The rotators are somewhat less affected. Beyond slight paralysis of the right inferior facial there are no bulbar symptoms. Bilateral ptosis is present, very marked on the left, much less on right side; the globes are practically immobile; the orbicularis palpebrarum is intact; the reflexes are normal; fundus: there is slight perivascular œdema of the optic discs, the margins being indistinct. Potassium iodide and mercury were used.

July 16.—The cervical muscles are less paralysed, also the ocular muscles, but the ptosis remains unaltered. Specific treatment steadily pushed.

August 10.—There is steady improvement, and greatly increased power in the cervical muscles. The muscles of eyeball are almost normal; the ptosis is very slight in the morning, but gets marked by mid-day.

August 20.—Movements of the head are normal, the ocular movements almost so. The ptosis is confined to the left eye and this only towards the end of the day; there is slight nystagmus. The mercury was stopped, iodide continued.

September 16.—Left the hospital practically well.

December.—Re-admitted for observation. Iodide has been continued. She has slight and transitory ptosis, but no other symptoms are observed. Discharged May, 1895.

July 31, 1895.—The patient was seen on this date, practically well.

November 20.—Third admission. Ptosis for two months reappeared on the left side, with slight diplopia, most marked towards the end of the day. Except for slight paralysis of right face, there are no other symptoms. There is no atrophy of the cervical muscles.

Case 32, Kojewnikov (30).—A male, aged 54, who had previously been healthy. There is no history of syphilis or alcoholic excess. The disease began suddenly some hours after a severe chill, when he first noticed weakness of the lips. Soon after he had a feeling of tightness of the face, difficulty in closing the eyes, in chewing, in swallowing, and nasal speech.

State.—The patient suffers at present from leftsided ptosis, weakness both of the upper and lower face, at times diplopia, limitation of the tongue movements, difficulty in swallowing (he had to be fed with a tube). He becomes easily tired when speaking, breathing is laboured, the face muscles are manifestly atrophied, both masseters, particularly the left, being very atrophic. The skin and deep reflexes are normal and there is no affection of sensation or of the special senses. At first he became worse, then he improved. Six months later after a chill the symptoms returned. There was then a slight difference between the pupils and slight insufficiency of the left internal rectus. The mouth was usually held half open and there was great tiredness of the muscles in chewing, speaking and swallowing. There were no electrical changes. The patient died suddenly, probably from paralysis of respiration, two and a half years after the onset of the disease. There was no autopsy.

Case 33, Kojewnikov (30).—A female, aged 17. No history of syphilis or alcohol. A brother has spasmodic asthma. Since the onset of menstruation in 1889 her health has been indifferent. Her present illness seems to have dated from this. She first noticed a difficulty in utterance and nasal voice. This continued till February, 1890, when she could neither whistle, blow out a candle nor expectorate, and was suffering from ptosis and difficulty of swallowing.

September, 1894.—There is weakness of the facial muscles, especially the lips; the lower lip falls. Speech is difficult and easily tires; the voice is nasal; there is left-sided ptosis. There is slight symmetrical wasting of the tongue. The soft palate is immobile. The muscles of the shoulder and hip are weak. Sensibility and the tendon reflexes are normal.

Summer, 1895.—There is defective taste and occasional diplopia.

September.—She is much worse; there is weakness of the extremities, an inclination inwards of both eyes, and difficulty in holding the head up—it falls forwards.

October.—Speech is worse, swallowing impossible.

October 14.—The right pupil is slightly the larger, she cannot firmly close the eyes mastication is very difficult. There is no atrophy of facial or masticatory muscles, but distinct atrophy of the tongue. The soft palate is almost immobile; defective adduction of the cords is seen on phonation; the posterior cervical muscles are weak and somewhat atrophied.

Electrical reaction; facial muscles show slight quantitative diminution to electrical currents. The soft palate does not respond to either current. In the tongue muscles A.C.C. is slightly better than K.C.C.

There is a distinct trace of sugar in urine; the patient has not menstruated since April.

Sensation is normal. She can only taste salt, and that imperfectly.

She is low spirited and very irritable.

The gravity of the symptoms varies, the muscular weakness being least marked in the morning.

October 26.—An attack of dyspnœa occurred during sleep at night, she was unconscious and cyanosed; it lasted three hours. She has had similar slighter attacks since.

November 1.—She improved from this date; sugar permanently disappeared from the urine on November 13.

December.—*In statu quo.*

In April, 1896, she left the hospital, still complaining of the chief symptoms.

Case 34, Toby Cohn (31).—A girl, aged 19, who has been ill for a year with weakness and tiredness in the arms and legs, ptosis, difficulty in swallowing, regurgitation of fluids through the nose, and nasal speech. All her symptoms are more marked towards evening.

On examination she was found to have double ptosis and lagophthalmos on both sides, a fixed expression with facial weakness on both sides; the jaw movements are feeble, the palate easily tired, speech is often nasal and difficult to understand, the letters *g* and *k* being especially difficult to pronounce. The tongue is normal, the neck muscles easily fatigued. The arms too are easily tired, and cannot be raised so well when sitting as when standing or lying. A similar condition of the lower extremities exists; after walking for some time a waddling gait develops as in the dystrophies. The knee-jerks are pretty lively. A paresis of the abdominal muscles exists. There is no ataxy, and sensibility is everywhere normal. The myasthenic reaction is very distinct; there are no other electrical changes. The internal organs are sound, the urine healthy, and there is no mental change. The family history is good; she had no preceding illnesses. An abnormal increase of the leucocytes is present in normal proportions.

Case 35, Kalischer (32).—A male, aged 64. No history of syphilis or alcohol. He had small-pox forty years ago, but otherwise his health has been good. In September, 1892, he developed double ptosis, paralysis of the extrinsic ocular muscles, and a week or two later paresis of all four extremities. A flaccid paralysis. The deep reflexes are increased, the skin reflexes lost; there is no atrophy or fibrillary tremor; the extensors are weaker than the flexors. There is no reaction of degeneration, but some diminution of faradic excitability in muscles and nerves.

There is no sensory disturbance, no sphincter trouble. The paralysis is always least in the morning. Later on the pupils became sluggish, particularly to light. Death occurred apparently from paralysis of respiration.

Post mortem.—Microscopical examination. The changes observed in the microscopical examination were numerous old and recent hæmorrhages, some large, some small, in the whole of the cerebral gray matter from the posterior part of the third nucleus to the sacral region.

There was degeneration in the nuclei and cells of the anterior horn all through the medulla and cord, varying in degree in different parts.

The position of the lesion did not correspond with the symptoms present during life.

Case 36, Widal et Marinesco (33).—A man, aged 31. Suspected of having tuberculosis. He developed severe headache, and in a few days the typical features of asthenic bulbar paralysis—ptosis, diplopia, weakness of external eye muscles, deep monotone voice, facial and palatal paresis, difficulty in chewing and swallowing, weakness in the neck and arm muscles, and the legs were easily fatigued. Typical variations in the intensity of the symptoms occurred. Dyspnœa and a small fast pulse were present. He died suddenly fourteen days after the commencement. For the last eight days the fever was 38-39°, and there was a trace of albumen in urine.

Post mortem.—The third, sixth, seventh and twelfth nuclei and cells of anterior horns examined by Nissl showed *chromatolysis*, the vessels were widened, there were no hæmorrhages; in the roots of the third, seventh and twelfth nerves degenerated fibres were seen by the Marchi method.

Case 37, Berkeley (34).—A male, aged 28, whose family history was good. When 14 years old slowness of movements attracted attention. His sister said, "When he stooped he never seemed able to get up again." Seven years ago the symptoms of his present illness were first noticed; he was easily tired and rather somnolent; he had an inordinate appetite. Four years ago he was troubled with vomiting after meals, which lasted for three or four months. Soon after he developed pronounced *deafness*, which persisted for several months, and has never entirely disappeared. His gait was clumsy and he was apathetic. Articulation was difficult and gradually became worse. A year ago the eyeballs became "stiff," and double ptosis with a peculiar facial expression appeared. There was no history of syphilis or alcoholic abuse.

State.—September, 1892. The facial expression is dull and heavy, the patient usually sits with his head bent forward because of weakness of the muscles at the back of his neck. The muscles of extremities are very feeble and easily exhausted. There is no atrophy or fibrillary twitchings. Sensation is normal; he is somewhat deaf. Bilateral anosmia is present. The pupils are semi-dilated and do not respond to light or accommodation. Deep reflexes increased, muscles react normally to faradism but are easily exhausted. Heart regular. Pulse fast (120). No albumen or sugar in urine. Incomplete double ptosis exists; the internal and inferior external rectus and oblique muscles of both eyes are paralysed. The eyes are practically immobile except that he can roll them upwards slightly. The masseters are weak and easily fatigued by faradism. There is weakness of the face muscles, the forehead is smooth, the orbicularis responds feebly, whistling is impossible, all the letters of the alphabet badly enunciated, the palate hangs low, the pharyngeal and palatal reflexes are well marked; no laryngeal examination was made. The tongue movements are defective. Contented disposition. Duration of illness ten years.

July 13, 1895.—While being fed with soup he *suddenly* choked and *died from asphyxia*; he had had no previous attack of dyspnœa.

Post mortem.—An old hæmorrhage was found in corpus callosum, having occurred probably in early life, perhaps when he had variola, aged 18 months.

This might account for the cerebral condition. No changes were present in the nuclei of medulla or pons, either in the cells or vessels; particular attention paid to third nucleus, but nothing abnormal found.

Case 38, Schlesinger (35). (*Very doubtful case.*)—A female, aged 29, admitted August 12, 1894, had had good health. Six weeks previously she became suddenly ill and experienced great difficulty in swallowing. Fluids especially were difficult to swallow, regurgitation through the nose took place, and there was a copious secretion of saliva which frequently flowed out of her mouth. There was frequent vomiting. After a few days she was better, but the arms and legs began to feel weak. Her condition gradually got worse.

State.—August 19, 1894. The mental state is normal, speech is slow and hesitating, the pupils are equal and react promptly. The eye movements are free, there is no diplopia, and no affection of the face, tongue, or larynx.

A high degree of general muscular atrophy is present. The muscles in shoulder region on both sides are both fairly markedly atrophied, particularly the posterior part of deltoid.

There is marked atrophy of the thenar and hypothenar eminences.

The arm-jerks on the right side are absent, on the left side they are very feeble. The muscles of lower extremities are much atrophied, but react to faradism. The knee-jerks are obtainable, but not increased, and sensation is completely normal except a large patch corresponding to the deltoid and right side muscles, where the sense of temperature is lost. There is retention of urine, requiring the catheter, and obstinate constipation.

Towards the end of August she became worse, vomiting and difficulty in swallowing developed, with increased salivation and rapid pulse. Tongue deviated to the left; the larynx was normal.

September 18.—Died from paralysis of the diaphragm.

Post mortem.—Nothing abnormal found; Weigert-Pal, Nissl, and Marchi all being used.

Case 39, Brissaud et Lantzenberg (36). (*Doubtful case.*) —A carpenter, aged 41, who had had bronchitis and pleurisy, noticed great general wasting after a cardiac illness (? myocarditis). One and three quarter years after the onset he had right facial weakness with inability to open the eyes to the full extent, a wasted, powerless tongue, double vision and weakness of the external eye muscles. Atrophy and weakness of sterno-mastoid and neck muscles, also in the arms and legs, with occasional fibrillary twitchings. Diminished knee-jerks, rough nasal speech and dry cough. Six months later there was a distinct improvement in most of his symptoms, except the fatigability of the muscles. No affection of swallowing. The jaw muscles, which were weak, now act well. No myasthenic reaction. Progressive improvement occurred. No statements as to ultimate result.

Case 40, Karplus (37).—A female, aged 24. Healthy family. When 5 years old she developed slight right-sided ptosis, which progressed. The following week the left lid was also affected. After a year the ptosis gradually disappeared. Since then every year for periods of several weeks ptosis has appeared, worse towards evening. There was occasional diplopia.

November, 1894.—She had ptosis, paralysis of the external eye muscles, weakness and tiredness of the upper and lower extremities.

December, 1894.—Paralysis of the external eye muscles. Paresis of the frontalis and ocularis; weakness in mastication.

After two months the weakness of the extremities disappeared and the ocular movements improved.

Autumn, 1896.—No ptosis; weakness of superior and inferior recti is present.

Case 41, Eulenberg (38).—A man, aged 28. Family history satisfactory. He had inflammation of the throat with a diphtheritic-like membrane a few months before onset of present illness; no syphilis; no excessive alcohol or tobacco history. In December, 1894, he saw double, and complete right-sided ptosis developed suddenly; later ptosis developed on the left side. In February, 1895, these symptoms disappeared, to reappear again gradually in November of 1895. From the middle of 1896 to the middle of 1897, he was again quite well. Since June, 1897, he has suffered from irregular cardiac action, ophthalmoplegia developed, and weakness of both arms and legs, especially on the right side.

State.—December 6, 1897. Complete ophthalmoplegia externa on both sides, the muscles are not all affected to the same degree. The right pupil is dilated and its reactions are sluggish; the papilla is of a whitish colour, but there is no disturbance of function (later the dilated pupils scarcely reacted at all to light); on the left side the optic nerve was hyperæmic; double facial weakness, particularly of the orbicularis palpebrarum muscle; movements of the jaw and palate are weak and deglutition is difficult; on the left side his ability to hear deep tones is diminished (insufficiency of the tensor tympani ?). There is weakness of the trunk and limb muscles which varies from time to time. There is striking increase of the muscular sensibility (*auffallende steigerung der muskelsensibilität*) in the limbs for electricity, especially for faradic currents. The myasthenic reaction is present in the extensors of the left forearm, the right extensor indices, and markedly in the interossei of the right side. Great improvement occurs after prolonged rest. There is no muscular atrophy; the reflexes are preserved; sensibility is intact.

Case 42, Mailhouse (39).—A male, aged 2¾ years. He has suffered greatly from the heat. A week ago he had a mild attack of diarrhœa a few days prior to the onset of the first symptoms.

July 6.—The child could not hold up its head properly, at other times the head was as erect as usual. There was no fever or vomiting, and no complaint of pain. He was unable to chew or to swallow properly, fluids tended to regurgitate through the nose. At times speech was affected so that he could not be clearly understood, at other times it was natural. He has not been confined to bed. The parents noticed that his eyes were half closed and that he could not smile. The family history was good.

State.—Marked bilateral ptosis, pupils and external eye muscles normal.

The face is expressionless, he does not smile, saliva runs out of the mouth. The mouth is half open, the soft palate normal, and the voice good. The reflexes are normal. After walking a short way he becomes unsteady on his legs, so that he asks to lie down. There is no atrophy. The electrical examination was unsatisfactory owing to uneasiness of child. The pulse 84; temperature normal. He was ordered to rest in bed and given strychnine and an intestinal antiseptic.

July 19.—Mailhouse was sent for because of peculiar rolling of the eyes; his mother thought he was weaker.

July 31.—Ptosis is gone; there is no strabismus; he can chew, swallow and smile, and runs about as he did before he was taken ill.

August 4 (*evening*).—A choking attack occurred during an attempt to swallow; weakness of neck muscles and regurgitation of liquids, &c., followed. He was better by the time the doctor got there.

August 5.—He has been up and down during day. While attempting to drink coffee from a cup a little difficulty in swallowing was noticed, his head drooped and he was dead.

He never had any attacks of dyspnœa; the heart's action was good.

There was no autopsy.

Case 43, Laquer (40).—A female, aged 21, whose mother died of phthisis. She had suffered previously from anæmia. She developed right-sided ptosis and double vision, and later difficulty in swallowing and regurgitation through the nose; ptyalism was present. Speech became indistinct and nasal; the arms and legs became weak. Three months before she had given birth to a child.

State on examination.—Left facial paresis; left-sided ptosis; weakness of the left internal and right external rectus, and diplopia; difficulty in whistling; speech slow, very indistinct and nasal in character; larynx normal. Tenderness on pressure over the fifth nerve on both sides. The knee-jerks were increased; there was shortness of breath. Great weakness in arms and legs was present, and often great difficulty in swallowing. The symptoms varied in intensity. The patient died suddenly one and a half years after the onset of her illness. The autopsy was negative, but there was no microscopic examination.

Case 44, Laquer (40).—A male, aged 49. Family history good. He has had pneumonia and repeated attacks of gout. He complained of pain and weakness in the right arm and leg; later, weakness in both arms. Double vision, ptosis, tiredness of the eye, face, and jaw muscles appeared; also of arms and legs. Fatigue of one group of muscles produced exhaustion in others, the myasthenic reaction was demonstrated in the biceps; there was no atrophy or bladder trouble, while sensation and the reflexes were normal. After an attack of bronchitis all the symptoms became intensified. His expression was that of a man falling asleep after the mid-day meal. Chewing, swallowing, and speech all showed early signs of fatigue. After glancing outwards and inwards several times the eyeball became fixed. There was no laryngeal affection.

Six months after its onset all the symptoms of the disease became much more pronounced. Distinct atrophy of the deltoid, biceps, triceps, pectorals, interossei, quadriceps, and calf muscles, developed. The tendon reflexes were brisk and could not be tired out. The myasthenic reaction was present. Some muscles, especially the gastrocnemii and extensors of the forearm, are tender on pressure.

Case 45, Wheaton (41).—Governess, aged 33, who had always been nervous. There was no neuropathic heredity. She had worked very hard. About the second week in July, 1896, she had a tooth extracted; the dentist told her that she must be very careful, or her gums would start to bleed and she might bleed to death. This frightened and worried her greatly. On July 21 she had a severe headache, in the morning she could raise the eyelids only with difficulty and the light pained her. On July 22, excepting for these signs and in addition ptosis and a slight increase of the reflexes, nothing abnormal was noted. During the next few days the ptosis became more marked, there was difficulty in chewing and in keeping the mouth closed. She was unable to sleep and had occasional attacks of palpitation. All the symptoms were increased by exertion.

August 14.—She had difficulty in walking, the muscles of the the neck were weak, menstruation began, and all symptoms increased in severity. She had difficulty in swallowing.

August 31.—She had a severe choking spell.

September 7.—To-day the patient had a bad spell of difficulty in breathing.

September 14.—She died in an attack of dyspnœa.

Mentally somewhat despondent. The reflexes increased gradually during the disease; there was no atrophy of the tongue and no tremors. The pulse was usually between 90 and 110.

There was no autopsy.

Case 46, Saenger (43).—A female, aged 22, seen December 29, 1896. She has been married one and a half years but has no children. Her previous health was good. Four weeks ago, she suffered from headache and sore throat. Difficulty in swallowing and double vision followed. Eye disturbance was present before the sore throat. The patient is anæmic and has a fixed facial expression. She has difficulty in preventing the upper lids from drooping. The eyes cannot be moved either inwards or outwards. The pupils are equal and react normally; she has difficulty in swallowing. The palate is weak. The voice is feeble. The pulse is somewhat rapid and regular. There is great diminution of power in both the upper and lower extremities; the gait is normal, but walking soon makes her tired. Now and again there is weakness of the neck muscles; the symptoms are more intense towards evening. Sensibility and the reflexes are intact; neither the myasthenic reaction nor reaction of degeneration are present.

January 1, 1897.—The patient is somewhat better, she still has pain in the spine and nape of the neck.

January 10.—She walks better.

January 13.—There is marked diplopia.

Subsequently she became pregnant and got practically well of the paralysis.

Case 47, Montesano (45).—A shoemaker, aged 17. Fourteen days after a cold bath, which he took when overheated, he was affected with weakness in the legs, so that walking was soon impossible; then fatigue appeared in the arms and trunk, and diplopia. The spleen was slightly enlarged. The muscles were very easily fatigued. There was inability to dorsiflex the hand, and to extend the fingers, deviation of the tongue toward the left and weakness of the left side of the face. The superior oblique and the external rectus of the left eye were paralysed. There is no affection of sensation. The faradic excitability of the muscles of the left half of tongue and right hypothenar eminence is diminished.

The myasthenic reaction is present in the lower extremities, especially in the quadriceps. Voluntary movement is still possible after exhaustion by faradism.

After four months the patient had recovered, excepting for slight diplopia and slight weakness in the finger movements.

The author suggests an organismal origin for the disease, the organisms becoming virulent in consequence of the above-mentioned chill.

Case 48, Kostetzki (47).—A male, aged 24, who had suffered from attacks of palpitation and dyspnœa, developed weakness in his trunk and extremities, so that he had to give up work. The voice became nasal, the breathing was uneasy. The symptoms gradually disappeared after a few weeks. Two months later, after a severe mental shock, difficulty in swallowing developed.

Present state.—The patient is very thin, his muscularity is feeble. There is bilateral ptosis, and the expression is mask-like. The muscles of the face are paretic. Movements are scarcely noticeable. The tongue can only be protruded very slightly. The pharynx and larynx muscles are paretic. Speech is indistinct and nasal; chewing is difficult, and he has difficulty in swallowing and breathing. There is paresis of diaphragm. Attacks of palpitation occur. Paresis and atrophy are present in various muscles of trunk and limbs—the pectoral, deltoids, thenar and hypothenar muscles, glutei and spinal muscles. The reflexes and sensibility are unaffected. The muscles are quickly fatigued (for example, diplopia develops after a few movements of the eyes). Improvement occurred after several weeks' treatment; a relapse then followed, and this variation in the symptoms recurred several times.

The author is of opinion that this case forms a transition variety between chronic bulbar paralysis and the so-called asthenic bulbar paralysis.

Case 49, Angelini (49). (*Doubtful case.*)—A man, aged 42, who had been nervous from youth. The illness commenced after emotional excitement, with tiredness of the muscles of the eye, the limbs and jaws. He also became soon fatigued after writing, speaking or reading, so that after a few words he could not remember what he had said. He had a severe feeling of pressure over the head and a feeling of stupor. After a short pause he could go on with his business. Sensation and the reflexes were normal. The myasthenic reaction was not present. Under hydrotherapy and strychnine the symptoms disappeared. Two years later there was a slight relapse from which he soon recovered.

The clinical picture shows an undoubted resemblance to myasthenia gravis. But while in this disease the symptoms are confined to the motor apparatus, in the case above described the higher functions were affected.

The case is more probably one of hysteria than myasthenia gravis (Angelini).

Case 50, Harry Campbell (53).—A governess, aged 28. Seen December, 1898. Twelve months ago she noticed she could sing in the morning but not at night, and since then she has gradually developed the symptoms she now complains of, *i.e.*, difficulty in swallowing; sometimes solids "stick in the throat," and fluids pass through the nose; nasal speech; a tired feeling at the back of the tongue. She cannot whistle, nor empty a spoon with the upper lip. There is upper facial weakness, but the corrugator supercilii acts well; great weakness of the orbiculares palpebrarum; after eating for some time the food tends to accumulate between the gums and teeth; mask-like expression; weakness of the face, soft palate and tongue. The above symptoms are all worse after using the affected muscles for some time. They are thus much better in the early morning than towards evening. No ptosis or diplopia. Knee-jerks and electrical reactions normal.

Later she complained of weakness in the arms, especially the right one; this she noticed in lifting her arms "to do her hair." This difficulty lasted a short time only and did not recur.

January 27, 1899.—All the symptoms much worse; she can scarcely close her eyes.

February 10.—Much better.

April 29.—Improvement continued until April 7; during last fortnight has been worse. Has had slight diplopia.

February 16, 1900.—The symptoms have fluctuated in severity since the last note was made, but the general tendency has been improvement.

Case 51, Sinkler (50).—A married woman, aged 37. Two brothers and a son suffered from nystagmus and rotatory head tremor, another son has nystagmus. There was no suspicion of syphilis. She had typhoid fever seven years ago, followed by bilateral ptosis, which lasted for four or five months. Two years ago she had diplopia. One year ago she was confined, the labour was a difficult one. A few weeks later swallowing and speaking became difficult, and weakness in the arms and legs developed. Since then at each menstrual period the symptoms have been worse.

State.—The face is mask-like, but there is no paralysis of the facial muscles. She can show her teeth and whistle. Speech is nasal and indistinct. After speaking for some time complete aphonia results. Deglutition is difficult, sometimes regurgitation occurs through the nose; the jaws soon become tired with chewing, as do the arms and legs after exercise, the gait becoming unsteady and shuffling. The knee-jerks are present and apparently do not become exhausted on repeated testing. All the muscles respond to faradism and the faradic irritability is not exhausted. There is no affection of sensation and no headache. There is partial double ptosis, the pupils react normally, almost complete paralysis in left external rectus, and partial of the left superior rectus exist. Patient is of a cheerful disposition. The fatigue which occurs in the eyes, throat, legs and arms is very characteristic.

Case 52, Punton (51).—A married woman, aged 25. She suffered from rheumatism before marriage. She has been ill for three years. Her only child was born just previous to the first symptoms; the labour was prolonged and difficult. She has never been well since delivery.

Diplopia, dimness of vision, and left-sided ptosis were the first symptoms. Mastication, articulation, and swallowing became difficult, voice became nasal, the tongue was less dextrous and felt numb. Weariness, prostration, and rapid heart's action followed slight exertion. She became unable to whistle, and strabismus appeared in both eyes. She developed a continuous lachrymation, and lost two stones in weight.

State.—The eyeballs protrude slightly and cannot be moved in any direction. She complains of excessive lachrymation during the waking hours. Double ptosis is present, left greater than right. She has diplopia; the facial expression suggests a putty-like blankness. Profound paresis of the face, right greater than left; she cannot whistle. The masseters are equally paretic, the bite is feeble, there is no atrophy, tremor or twitchings. The tongue is thick, flabby, and completely devoid of lateral movement. The palate moves very little. Speech is thick, indistinct and nasal, and deglutition of solids difficult, while fluids regurgitate through the nose. The left vocal cord is paralysed, the power in the extremities is normal; there is no atrophy, and no twitchings or sensory symptoms; the superficial reflexes are normal, the deep are slightly exaggerated. There is no ankle clonus; electrical reactions are normal; urinary analysis negative. The pulse 90, regular.

Case 53, Clifford Allbutt (52).—A girl, aged 18. The personal and family history are good. She caught cold, followed by stiffness of the tongue and jaws, which disappeared after a few weeks.

Six months later she was seen by Clifford Allbutt. She spoke oddly, "as if with a potato in her mouth;" when she tried to read a book she began well, but soon the disorder set in and she became unintelligible. Her friends said that she read much better when at home quietly. A few weeks before she had begun to have difficulty in swallowing. "She choked over her meals, more when she was tired." There was no evidence of hysteria or of organic disease observed, except that the forefinger of the left hand seemed weak and fumbling. She moves her tongue and jaws and all the muscles of the face, throat and orbit quite normally. The palatal reflex was normal. A provisional diagnosis of hysteria was made. Under treatment she improved very much. One evening the symptoms became worse, especially the swallowing, and her mother spoke to her somewhat sharply. Next morning she went to her mother's room to protest, when she suddenly fell to the ground, was convulsed, turned blue and died. There was no autopsy.

Case 54, Seiffer (54).—A female, who has been ill eight years (age not given). The illness came on without known cause. Five years ago the fatigue in the arms and legs, which was present before, became more marked, her gait became waddling, jaw weakness and ptosis developed. The tiredness was always more marked towards evening.

State.—She has double-sided ptosis; the eye muscles act normally, but at times nystagmoid movements are present. The patient quickly becomes tired on trying to count aloud, ultimately she is quite unable to do so. She can only raise herself with difficulty from the horizontal position. The arms if held up quickly become tired, as do the legs after walking, when she wavers and ultimately staggers. There is a distinct myasthenic reaction; nothing peculiar as regards the blood is present.

Case 55, Buzzard (55).—A schoolmaster, aged 40. His paternal uncle died in a lunatic asylum, a paternal aunt died of creeping paralysis; there is no history of syphilis or alcohol. Seven years ago, after taking cold baths, the little and ring fingers of the right hand felt weak. This recurred from time to time; nasal voice, feeling of constriction in the throat and ptosis followed. During the year 1895, excepting the weakness in the right index finger, he had no trouble; legs and arms then became weak, and later there followed diplopia, weakness in the tongue and jaws, difficulty in coughing and in masticating, attacks of dyspnœa and palpitation, fatigue; cold weather and mental excitement all increase the intensity of his symptoms.

On admission.—Very intelligent man, indistinct nasal speech, diplopia, right-sided ptosis, upward movement of eyes defective, both external recti weak, pupils react perfectly, jaws easily tired, double facial weakness (especially upper face), tongue moves freely but easily exhausted, palate movements and reflex power poor. After repeated deep respirations the glottis finally opened less than at first. Great weakness of the neck muscles, arms and legs are weak, he has difficulty in dressing himself and cannot walk more than half a mile, no muscular atrophy, no fibrillary twitchings, myasthenic reaction present, no impairment of sensation, no sphincter trouble, arm-jerks poor, knee-jerks active, not exhausted by frequent tapping, nothing abnormal in the urine, other organs healthy.

While in hospital patient improved greatly, but a relapse occurred without apparent cause, the relapse characterised by the preponderance of severity of symptoms in the trunk and muscles of the extremities rather than those of the bulk.

Case 56, Buzzard (55).—A female, aged 24, housemaid. Rheumatic family history; no nervous disease. Anæmic for eighteen months, otherwise good health until a year ago. First symptom was giving way of the legs when walking upstairs, legs have been weak ever since; soon after arms became weak, speech became nasal, ptosis developed, diplopia, difficulty in mastication, in coughing and in swallowing were noticed; no attacks of dyspnœa or palpitation. When excited, symptoms are intensified; cold does not affect her; the symptoms are no worse at the menstrual period. On admission, no alteration in mental state, no affection of cranial nerves, speech almost normal at first, after reading aloud soon becomes indistinct and nasal.

Double ptosis, left pupil greater than right, ocular movements good, slight nystagmoid movements on extreme lateral deviation, convergence poor, orbicularis palpebrarum very weak, power of mastication very poor, so feeble that she cannot hurt a finger introduced into the mouth when she tries to bite it, tongue and palate movements fairly free but soon exhausted, extremities weak, no atrophy, no fibrillary tremors, myasthenic reaction demonstrated in biceps, sensation and sphincters unaffected, deep reflexes active. Knee-jerks cannot be exhausted by repeated tapping.

Case 57, Feinberg (57).—A man, aged 44, with no neuropathic heredity, developed obstinate constipation, with symptoms of obstruction, colic, meteorism and vomiting. On the fifth day he had severe pain in occiput and region of upper dorsal spine, followed by numbness and weakness in the extremities, double ptosis, immobility of the eyeballs, feeble power of movement in the tongue and lips, inability to wrinkle the forehead, indistinct speech, continuous salivation, difficulty in chewing and swallowing, the latter only to a slight degree. The patient soon began to improve quickly.

State a month after appearance of symptoms.—A strong man. He has slight double ptosis, the ocular movements were slow, the up and down movements being defective, there was no nystagmus, the pupils react normally. The right side of the face is paretic, the left normal except for slight weakness in the left frontalis. Attempts at whistling and showing the teeth gave poor results. Speech is distinct with the exception of the labials, the tongue moves well, the power of biting is feeble on the left side. The palate moves well, the reflex is normal. There is no increase in the rate of the pulse or respiration. The occipital headache and pain in the back have long ago disappeared. All the other organs are normal; the urine contains nothing abnormal. The patient complains of great weakness and muscular prostration. There is no muscular atrophy and no disturbance of sensation. The knee-jerks are increased. There is no ankle clonus and no rigidity. He can make all movements, there is no ataxy. A feeling of tiredness is present even when he lies in bed, which is exaggerated when he stands or walks. There are no electrical changes.

Six weeks from its onset nearly all symptoms of illness had disappeared; since then he has remained well (a year).

Case 58, Leonard Guthrie (56).—Waitress, aged 23. Her previous health and family history were satisfactory.

Her illness commenced two years ago with difficulty in speaking; later, difficulty in swallowing, nasal regurgitation, inability to close the eyes and weakness in the hands appeared; all the symptoms were worse after exertion or excitement.

State.—A delicate-looking girl, but not markedly anæmic. Paresis of the orbicularis oculi and oris, tongue, soft palate, and probably of the pharynx. There is upper facial weakness but no ptosis, the ocular movements are perfect, there is no nystagmus. The pupils react well. She cannot blow out her cheeks or whistle; speech is indistinct and nasal. The vocal cords act normally. Deglutition is difficult; the jaw muscles are weak. She has fair power in the extremities, but soon becomes exhausted. Sensation and the sphincters are normal. The myasthenic reaction is present. There is no muscular atrophy. After five weeks she was much improved.

Case 59, Raymond (59).—Woman, aged 25. Entered February 7. Dead child in October last.

January 8.—Took cold, was seized with paralysis of left infrafacial same evening, but Raymond is not certain whether the right facial escaped.

January 25.—Ptosis supervened (left); eight days ago right ptosis—this less. This paralysis is intermittent and almost disappears at times. Ptosis worse second part of day.

Towards February 7, complained a little of diplopia with difficulty in mastication. This fatigues her, has to stop every few "chews," due largely to paralysis of masseters, especially left; difficulty of protruding tongue, applying it to palate, and speech is *trainante;* labials ill pronounced; after speaking short time speech gets thick and less distinct. Intellect perfect; speech slow. Pupil reactions normal. Fundus normal. No sensory trouble. Reflexes normal. Patient complains of getting tired easily, and of not being able to walk for long.

Treatment.—Faradisation of paralysed muscles, sulphur baths and cold douches.

Improvement from February 26. April 15, cure complete.

Pflüger (gives no reference) (*Gazette des Hôp.*, 1,168), has cited a case of ophthalmoplegia externa consequent to menstrual trouble. (*De Graefe*, Landsberg, Schœler.)

Case 60, Harry Campbell (unpublished).—A girl, aged 19, who after an attack of scarlet fever three and a half years ago became paralysed all over (she could not even turn in bed). During the following year she gradually improved, and recovered power all over excepting in the face, which felt stiff. About twelve months ago she gave birth to a child. During pregnancy the face improved, but became worse again during lactation, which lasted for seven months.

On admission her chief complaint was a constant running of water from the eyes.

There is marked double facial weakness affecting both the upper and lower face; great weakness of the orbicularis oris and palpebrarum; occasional diplopia, and the eyelids often droop towards evening. There is no affection of the soft palate, tongue, or larynx, and no weakness of the extremities. The condition is worse at the menstrual periods and in cold weather. The knee-jerks are brisk; all the muscles react readily to weak faradic currents. There is no affection of sensation.

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A CASE OF ASTHENIC BULBAR PARALYSIS (MYASTHENIA PSEUDO-PARALYTICA GRAVIS).

BY ARTHUR J. HALL, M.A., M.B., M.R.C.P.

Professor of Pathology, University College, Sheffield; Hon. Physician, Sheffield Royal Hospital.

MRS. X., a multipara, 44 years. Comes of a nervous stock, and herself suffered from migraine. Father lived to 81; mother alive, 85 years of age, healthy, but of low nervous tone. One sister has melancholia, two others have severe migraine. Has had two children, labours quite normal, last about twelve years ago. No history of syphilis. Menses regular, painful, latterly profuse. Has lately suffered a great deal from domestic worry on account of the presence in the house of a relative whose mental condition for the last two years has been particularly trying.

Present illness.—Early in December, 1896, the patient complained of weakness in all her muscles. She always seemed tired, and could not even hold a tea-cup for long at a time. On Christmas Day she had some swelling of the left side of the face, thought to be due to exposure to cold; at the same time slight ptosis of the left eye was noticed. The ocular muscles at this period acted perfectly regularly. After this the ptosis was frequently noticed to come on during the day and increase towards evening, whilst absent first thing in the morning. The general weakness increased, and about the beginning of February she fell down and bruised her head, apparently from weakness of her legs, as she had no vertigo. For the last few days she has remained in bed and has hardly been able to raise herself. She has some headache, no vomiting, says things appear all out of shape.

Present condition, February 11, 1897.—She lies in bed, looking languid and depressed. There is marked ptosis of the left eye and slight on the right side also. The ocular muscles act irregularly, especially in the associated movements of the left internal and right external rectus; the amount of irregularity varies from time to time, but the patient is so quickly exhausted that I found it beyond me to say exactly what muscles are actually affected. The left internal rectus is, however, the most distinctly feeble. The grasp of the hands is feeble, but equal on the two sides. She is generally unable to stand or even to sit up by herself, but at times can both sit up and even walk quite well.

There is no wasting, no loss of sensation, no loss of control over the sphincters. The viscera seem normal in all respects.

The tendon and superficial reflexes are quite natural; there is no clonus. Speech is slow and drawling, the voice feeble as though she were tired. She has never had any choking, but often complains of being too tired to finish eating what she has begun, and complained of considerable difficulty in swallowing. The ophthalmoscopic examination was negative.

Electrical reactions perfectly normal.

I was puzzled as to the exact diagnosis. I did not find sufficient data for diagnosing any definite lesion, and was yet unwilling to call the case purely functional. At the end of a week I saw her again, and found her somewhat more cheerful and on the whole slightly improved by her rest. As she lived some distance from Sheffield we arranged that she should come into a private nursing home and try the effect of isolation, overfeeding, electricity and massage.

She came into the home towards the end of February. I saw her almost daily, and for the first two weeks she improved very greatly in every respect. She was much more cheerful, took her food well, and had less ptosis. She was also able to move herself in bed far better. In fact the result of treatment seemed most satisfactory. At this point a menstrual period came on, which lasted ten days and was very profuse in quantity. During and after this all the improvement of the past two weeks disappeared and she was just as bad as ever she had been. I hoped that this might be only temporary, but unfortunately these hopes were vain. She got steadily worse in every respect, and I felt convinced that there was some serious organic nervous disease. I asked my colleague Dr. Burgess to see her with me, which he kindly did, and we agreed that there seemed no prospect of her improving under the present treatment and that she had better go home, for she was now extremely depressed. As regards her symptoms at this date, they were as follows :—

Extreme mental depression. General weakness of all her muscles. Marked ptosis of left eye. Paresis of ocular muscles varying in extent from day to day and very difficult to determine, also the eyes frequently moved unequally when she was asked to look at any particular object. A marked nasal tone in the voice.

All these conditions were very much worse when attention was drawn to them. The patient herself noticed this, and the nurse assured me that the nasal character of the voice would be quite absent for a long period until I came, when it would begin at once. The patient also told me one morning that she had difficulty of breathing on first waking, but that it was not severe, and the nurse had not noticed any real dyspnœa. These attacks of dyspnœa were repeated two or three times.

On April 2 she went back home, and stood the journey, a distance of five miles in a carriage, very well. She slept well and seemed bright and talkative next morning. She had some difficulty in swallowing her breakfast, and after doing so she went rather blue and made a curious "rattling" in her throat. She soon recovered and seemed no worse for this. At about 1 p.m. she had some beef-tea, after which she suddenly began to have dyspnœa, became cyanosed and rapidly collapsed.

I went out immediately and at 2.30 p.m., when I saw her, the condition was as follows:—

She is lying on her back with jaw dropped; ashy gray colour, extremities blue and cold. Eyes half open, occasionally widely opened and rolling about; pupils small, equal, do not react to light. Respirations very short and spasmodic, stertorous, infrequent, cheeks drawn in at each inspiration. Pulse 100. Heart's action somewhat tumultuous. Urine passed into bed. Can articulate "Yes" and "No" when spoken to. All possible remedies were tried but she gradually became comatose and died at 5 p.m.

I was very anxious to clear up, if possible, this extremely sudden and unexpected ending, and was allowed to make an examination of the cranial contents only on April 5. This I did with the help of Drs. Burgess and Cocking, and so far as the brain and medulla oblongata were concerned a careful naked eye examination revealed absolutely nothing in any part of the membranes, vessels, or nervous tissue, which could be distinguished from that of a perfectly normal adult.

I kept the whole of the pons and medulla and portions of the cortex cerebri and cerebelli for microscopical examination. These were hardened in Müller's fluid, cut in celloidin and stained by Weigert's method, aniline blue-black, alum carmine, &c. A careful examination of a large number of sections failed to reveal any changes in the nerve-cells or fibres, or in the interstitial tissue or blood-vessels.

Reviews and Abstracts.

Ueber die Raumwahrnehmungen des Tastsinnes. By Dr. Victor Henri. Berlin. Reuther und Reichard, 1898, pp. 226.

M. Henri believes that experimental psychology has now reached a stage of development at which the critical collection of the results gained in its various departments is necessary for further progress. In the present memoir he has written a valuable account of our present knowledge of the psychology and physiology of tactile spatial perception. M. Henri is already well known for his original contributions to this subject, and his account of these make the book much more than an epitome of previous knowledge. Perhaps the most valuable feature of the book is the training which it suggests in psychological methods. The experiments described are very simple, and require very little apparatus, and that only of the simplest kind. Their careful repetition would, however, give considerable insight into the methods and characteristic features of psychological experimentation, while the experiments themselves throw light on several questions of great importance in relation to disputed psychological and philosophical problems, such as to the nature and mode of genesis of spatial perception. In the present state of psychology it is very important to separate facts from theories; nearly all psychological work is done with a bias in favour of some one school of thought, and it is often no easy matter to sift out the positive contributions to knowledge from such work. This task the author has successfully carried out. The first part of the memoir is devoted to the facts which have been more or less firmly established by experimental research, while in the second part the theories of spatial perception are reviewed in the light of these facts.

The facts are considered under two heads: (1) The perception of spatial relations by means of touch, and (2) localisation of a point on the skin. The author distinguishes sharply between these two processes, and bases this distinction partly on pathological evidence, stating that the two processes may be very differently affected in such a condition as tabes dorsalis. The actual observations given on this head are very scanty; one case is described in which localisation on the foot was normal, while the spatial threshold was enormously increased (7-9 cm.). Further observations in this direction are needed. Of the original contributions of the author two may be especially mentioned. He has shown that the familiar illusion with crossed fingers described by Aristotle is only one example of a general law that in unusual positions of the fingers (and other parts of the body), the localisation and spatial relations of touched points are the same as if the fingers (or other parts) were in their customary positions. The second contribution is an original method of studying localisation. The ordinary method has the great disadvantage that apparent inaccuracy of localisation may be partly or wholly due to defect of the localising movement. M. Henri advocates localisation on a life-size pattern or model of the part of the body which is being investigated, and obtains satisfactory results. So far the method has been very little used in pathological cases, but with patients of ordinary intelligence should prove useful. He finds with this method that the errors of localisation tend to occur in definite directions; on the limbs a touched point is localised too far in the direction of the nearest joint. This result is ascribed to a tendency to localise in reference to certain fixed points, and the errors were found to decrease the more nearly the touched point approached such a point of reference. The observations of Mr. Victor Horsley on erroneous localisation in cortical disorders, which are very interesting in this connection, appear to have escaped the author's attention.

The author seems also to have paid insufficient attention to pressure-points. According to Goldscheider these points form the basis of tactile spatial discrimination, but the results of this worker are dismissed in a few lines as being based on minimal values, not comparable with the mean values of other observers. If Goldscheider is right, the stimulation of pressure points affects the specific nerve endings which have to do with spatial discrimination, and the existence of such specific organs is hardly a matter which can be lightly passed over in a book of this kind.

In the second part the author gives an excellent account of the various theories of spatial perception. The popular view that the perception of spatial relations is wholly dependent on movement, has, of course, as little foundation in the case of touch as in that of sight, and M. Henri points out various facts which contradict the modified view held by Wundt and others, that spatial perception depends on a psychical synthesis of tactile and muscular elements.

In Aristotle's illusion, for example, the sensations arising from the altered positions of the fingers wholly fail to influence localisation in the way they should according to this view. The author refuses to range himself with the advocates of either the genetic or nativistic views. He points out facts like the above which are irreconcilable with the genetic theories at present in the field, but, while inclining to the nativistic position he refuses to adopt it, because it has not (it probably never can have) a positive experimental basis.

W. H. R. Rivers.

St. John's College, Cambridge.

The Education of the Central Nervous System. By Reuben Post Halleck, M.A. (Yale). Pp. 258. Macmillan and Co., London and New York, 1896.

In this book attention is called to the importance of early training of the central nervous system while its brief period of plasticity lasts, and the author says his principal object in writing it is "to prescribe for our complex central nervous systems, at the proper time, the special kinds of exercise—sensory, motor, and ideational—demanded for full development." In the first chapter a short description is given of nerve-cells and nerve-fibres, the spinal cord, medulla oblongata, cerebellum, and cerebrum, including a brief account of the motor and sensory centres, and the projection, commissural, and association fibres of the brain. The fatalistic aspects of education are alluded to, and refuted by, the author, who says that he has demonstrated that young nerve-cells are more amenable to training than any other matter of which he has knowledge, and there is no doubt that careful culture can do much in children who have a healthy mental condition. If we ask how brain tracts can be modified, the answer is, through the action of sensorial impulses, motor movements, and especially by the development of the fibres of association, for without these there can be no memory, association, and motor discharge. The importance of training the faculty of attention is rightly insisted upon, and it is shown that the nerve-cells must be well nourished, in order that this faculty may be maintained at its highest point of development. As regards environment, it must afford sufficient stimuli to develop the senses, and allow for motor action in the growing nervous system. For this purpose a life in the country is preferable to one in town. As regards age, training should begin early, but we question the author's statement that no one gets a new idea into his head after the age of thirty-three. The author rightly lays stress upon the importance of training the senses, and in chapter viii. he gives a list of objects for developing the olfactory, gustatory, auditory, and visual tracts, and the sense of touch. An interesting account of how Shakespeare's senses were trained is given, from which we learn that though he left school at the age of fourteen, he had roamed from childhood in the fields and forests that surrounded Stratford-on-Avon, and in this way developed his various senses. Passages are quoted to show that he not only observed natural objects, but human beings as well. In chapter ix. is shown the importance of recalling images of sense-objects as a means of educating the nervous system, and the fact that these images are necessary aids in further modifying and developing the sensory cells is demonstrated. The book will be useful to parents, teachers, and all who are interested in the education of children.

L'Epilepsie. Par le docteur JULES VOISIN. Pp. 420. Paris, 1897.

THIS book consists of a series of lectures given by Dr. Voisin at the Salpêtrière. The author first mentions the numerous definitions which have been given to this malady, and says, quite truly, that it is not a true disease, but a collection of symptoms which are more or less developed in one individual. He believes that heredity, which plays such an important part as a predisposing cause in the production of mental and nervous affections, scarcely acts directly in this affection, but is more active in what he calls "transformed" heredity. From a statistical table which the author gives, it appears that heredity, acting directly, only accounts for 9 per cent. of the cases, while the transformed heredity of tuberculosis and alcohol accounts for 28 and 31 per cent. respectively. Among the determining causes the author places sleep as the most frequent factor; and it is due to the occurrence of the fits in the night that the patient and his friends are ignorant that he suffers from them. As is well known, they occur most frequently in the early morning, owing, as the author believes, to the blood being charged with toxines. At any rate, it is a fact that when epilepsy commences, it occurs during the night, and it is only when the patient has suffered from the affection for some time that it occurs during the day. The author proceeds to discuss the remote and immediate premonitory symptoms, the auræ; the symptoms and different varieties of the attack and their groupings, as well as the symptoms which occur after the attack, such as dulness, dementia, and epileptic mania. Dr. Voisin has noticed that in many cases there is a disturbance of the gastro-intestinal apparatus previously to the attack, and when this disappears the patient returns to his normal condition; hence he believes that a great number of cases are of infectious origin, and are due to toxines circulating in the blood. On examining it after an attack, he observed that it was not only black and pitch-like in appearance, but there was a reduction of the activity of the oxyhæmoglobin and a diminution of the red globules, besides other changes. He made a bacteriological examination of the blood, and found in two cases a staphylococcus similar to that which had previously been noticed by others, in the blood of patients who had suffered from eclampsic convulsions. He therefore thinks that the epileptic fits are produced sometimes by autointoxication and sometimes by the products of the staphylococci, which have not been sufficiently eliminated. As regards arterial tension, he noticed that it became reduced before the paroxysm and rose above the normal condition as soon as the period of stertor commenced. On examining the urine, he discovered that post-paroxysmic albuminuria existed in half the cases, and was met with in all varieties of epilepsy, that the epileptic state was always accompanied by albuminuria, but that it disappeared quickly and was very variable in quantity. He also examined the urine to ascertain its toxic character after the attack in various individuals, and noticed that the urine collected twenty-four hours after the paroxysm was of a volume considerably above the normal, urea was increased, phosphates were in excess, and peptones were almost always present. In addition, he isolated a body which was extremely toxic when injected into animals, and concluded that the urine is hypotoxic before and during the attack, and is hypertoxic afterwards. The author then goes on to discuss Jacksonian epilepsy, the spasmodic hemiplegia of infancy, the progress, diagnosis, prognosis, pathology, and treatment of epilepsy, and winds up with certain medico-legal points as to the responsibility or otherwise of patients suffering from this affection. Those who are interested in and have to treat this malady will find the book useful.

FLETCHER BEACH.

Two Cases of Hereditary Cerebellar Ataxia.—By K. Miura (Mittheilungen der Med. Facultät der Kaiserlich-Japanischen Univ. zu Tokio, Bd. iv., Heft. 1, 1898).

Case I.—Monojiro Niwa, a man, aged 37. Father died of cerebral hemorrhage; mother of hereditary cerebellar ataxia in 42nd year. Sons of a cousin of the mother said to have had the same disease. Patient's gait affected in 25th year; a temporary affection of hands in 30th year. After a febrile attack in 33rd year co-ordination worse, speech and sight involved. Increase of symptoms in 36th year caused him to stop work. On admission to hospital expression stupid, excessive facial movements in speaking, slight tremor of tongue, speech explosive, stammering, linguals specially indistinct, sputtering when speaking, pupil reaction sluggish to light and accommodation, slight horizontal nystagmus, field of vision contracted on both sides and unequally, injection of optic papillæ, with slight clouding of margins, vertebral column fairly straight, swaying of body when sitting, no muscular atrophy, imperfect co-ordination of upper and lower extremities, great difficulty in balancing on legs, reflexes unaffected, sensibility intact. The writing, a specimen of which (Japanese) is given, is said to show marked ataxia. During the few months that patient was in hospital before death supervened, symptoms of beri-beri developed, viz., lowering of sensibility in trunk and inferior limbs; sensation of pressure in epigastrium, sensitiveness to pressure in calves, vomiting, with other digestive disorders, slight œdema of legs, almost total disappearance of knee-jerks, slight rise of temperature.

The results of the autopsy are given with great detail. In the nervous system the chief points concerned the loss of bulk in certain parts, especially the pons, medulla, cerebellum, and cord. The pons was diminished in all directions, measuring 22 mm. in length, and 27 in breadth, instead of 29 and 36. The loss of bulk appeared to be due to a diminution in the transverse cerebellar fibres. The medulla oblongata was 19 mm. long by 18 mm. broad above, 16 mm. broad lower down, instead of 23, 27 and 18 respectively (according to Krause). The cerebellum weighed 80 gr. instead of 169; its volume was 72 ccm. instead of 162. (From some hitherto unpublished figures given by the author, Prof. Taguchi makes the average Japanese brain somewhat smaller than the European). No change beyond this of size could be discovered by careful naked eye and microscopic examination. The spinal cord was diminished too, being flattened from before backwards. At the 6th cervical root it was 12 × 7 mm. instead of 12·4×9·5; at the 6th dorsal root, 8×5 instead of 8·5×7·3, and so on. No degenerative change in columns or cells, nor in the spinal roots. The complication of beri-beri accounted for degeneration of nerve fibres in peripheral nerves of the lower extremities.

Case II.—Kentei Niwa, 41 years old, elder brother of foregoing. No syphilis; alcoholic and licentious in habit. After a febrile attack in March, 1888, lasting ten days, he noticed uncertainty in gait, awkwardness of hands, affection of speech and eyesight, &c. After some improvement, he got worse in 1890-91.

Condition in June, 1896: Hearing defective, speech stammering, jerky, explosive, worse when talking to strangers, tremor of tongue when put out, tremor of chin on bringing the mouth to a point, eyeballs small, no nystagmus, reaction of pupils normal, field of vision irregularly contracted, optic discs somewhat clouded, impotence since illness began, hands tremble on being stretched out, loss of power in hands and arms, ataxia in these parts (touching points, writing), similar ataxia, only more evident, in lower limbs, "drunken" gait, reflexes not affected, diminished sensibility on outer side of leg below knee.

A year later, all the symptoms had become worse; knee-jerks nearly absent, facial muscles acting in excess in speaking or opening mouth, micturition delayed. He was still able to attend to his business of ragman.

PROCEEDINGS OF THE NEUROLOGICAL SOCIETY OF LONDON.

At the Clinical Meeting held at 11, Chandos Street, on Thursday, June 21, the following cases were shown :—

(I.) Dr. H. Head, F.R.S.—*Two cases of muscular atrophy confined to the upper extremities, probably of neuritic origin.*

(1) Mrs. C., aged 26. She was in perfect health until November, 1897. She was then six months pregnant, and a saucepan of boiling water was upset over her right hand, scalding her badly. Two months later she had a pricking feeling in the left hand which began to waste steadily. About May, 1899, one month before her last baby was born, the right hand began to waste. This wasting was preceded by a feeling of pins and needles in the hand. In August, 1899, the left hand showed marked wasting of the thenar, hypothenar and interosseous muscles. The fingers were over-extended at the metacarpophalangeal joints. The condition of the right hand was the same, but much slighter in degree. The reaction of the affected muscles to faradism was distinctly diminished. No other muscles in the upper extremities were affected except the lower part of the right trapezius, which appeared to be slightly wasted. When her arm was raised to the horizontal position the right scapular border projected distinctly, but the deformity disappeared immediately her arm was raised above the horizontal. In this case sensation was distinctly affected. Touch and pain were not obviously affected, but heat and cold were lost over the palm and fingers of the left hand and to a slighter degree over the palm of the right hand. The loss to cold was more certain than the loss to heat. The reflexes and pupils were normal and there were no other signs of disease. She slowly improved, but the wasting of the hands is still evident and the lower part of the trapezius appears to be slightly affected on both sides, especially on her right. Sensation is now perfect.

(2) Florence R., unmarried, aged 25. About October, 1898, she had a good deal of pain in the left supraclavicular fossa, accompanied by numbness, coldness, and "pins and needles" in the left arm and hand. About four to five months afterwards she began to notice that she dropped things from the left hand. In October, 1899, the interossei of the left hand were markedly wasted and the hand was distinctly clawed. Both thenar and hypothenar muscles were somewhat wasted and flabby but no movement of these groups was absolutely lost. There was some doubt as to whether the right hand was wasted at this time. There was distinct slight loss of sensation to heat and cold over an area on the radial border of the left forearm and hand, including the thumb. No alteration in touch or pain could be discovered. There were no other signs of disease. The pain continued in the left shoulder and back of the neck and she had occasional pain in the right arm and hand. Now both hands show marked wasting and the lower trapezius on the left side is wasted. The only loss of sensation is a slight loss to heat and cold over the tips of the thumb and forefinger of the right hand. The electrical reactions are markedly altered in the small muscles of the left hand and to a slighter extent in the lower part of the left trapezius.

(II.) Dr. COLMAN.—*Case of "ophthalmoplegic migraine."*

Ida E., aged 14. Father has had rheumatic fever. Nothing else relevant in family history. The first attack when aged 11. There was slight ptosis without pain and twitching of the eye and forehead for a day or two, then severe headache and vomiting lasting for three weeks. At the end of that time ptosis was complete. After the attack the ptosis diminished but did not pass off. There was also external squint and diplopia.

There was a second attack of headache and vomiting three months later, and several slighter ones followed, without any increase in the ptosis. Since a severe attack in December, 1898, the ptosis had been constant. The ocular movements could all be performed in the left eye, though weakly. There was slight external strabismus when at rest, the eye looking a little downward as well as out. There was diplopia on looking to the right only. The left pupil is contracted and did not react to light or dilate to shade. There was, however, wide dilatation on her attempting to look upwards. The fundus was normal. Her general health was excellent. The attacks had been slighter and much less frequent during the last eighteen months, during which time she has taken bromide of potassium and tincture of gelsemium regularly.

(III.) Dr. D. B. Lees.—*Case* 1.—*Hæmatomyelia ?—partial recovery.*

Man, aged 47, admitted March 9, 1900. Three weeks before admission fell backwards, striking the lower part of his back. Felt severe pain and had to be assisted to walk home. Pain was in lumbar region, also between shoulders and over metacarpo-phalangeal joints of right index and middle fingers. Limbs very weak (especially right arm and leg) but not paralysed. Great effort in passing urine and fæces.

On admission, three weeks after onset.—(1) *Sensory.*—*Pain*, lower lumbar and sacral regions; also in right hand, over second and third metacarpo-phalangeal joints. *Hyperæsthesia* marked over lower lumbar and upper sacral regions. *Anæsthesia* over right hand and forearm; some over left hand also. *Complete sensory loss* (touch, pain, temperature and sense of position) over whole of both lower limbs; upper limit of anæsthesia 3 inches above symphysis pubis. (2) *Motor.*—*Right upper limb :* Decided wasting of interossei. No power of flexing the extended fingers, or of approximating thumb and little finger. Grasp very weak. Weakness of extensors of wrist. Some weakness of flexion of elbow. No wasting of arm or forearm. *Left upper :* Some wasting of interossei, but can flex extended fingers. Grasp stronger than right. Slight weakness of extension of wrist. *Right lower :* Weakness of all movements; no wasting. Right foot in position of talipes equines; cannot be dorsiflexed. *Left lower :* Stronger than right and foot can be dorsiflexed. No wasting. *Reflexes :* Knee-jerks very exaggerated, especially right. Suprapatellar jerks very marked. Ankle clonus on both sides, especially right. *Eyes :* No paralysis of external ocular muscles. Pupils equal, react to light and with accommodation. Discs normal. *Syphilis* (?) *:* Had gonorrhœa and bubo in right groin at 16. Scar in right groin Two white scars with pigmented margins on left leg.

Treatment.—Pot. iod. gr. 20, liq. hyd. perchlor., ʒj. t.d.s.

March 16 (*one week after admission*).—Improved; sensation over lower limbs restored, with a feeling of "pins and needles" in them. A touch or pin-prick at any part of lower limbs or trunk (up to second rib) causes a burning sensation. Anæsthesia now limited to skin over three middle metacarpo-phalangeal joints (dorsal and palmar aspects) of right hand

and over whole of index of left hand. Inco-ordination of right upper limb still present. Knee-jerks and ankle clonus less. Plantar reflexes not obtained. Much more power in lower limbs; still cannot dorsiflex right ankle. Slight increase of power in right upper limb. Can flex extended fingers. Able now to write. Still difficulty in urination and defæcation. No bedsores. Slight ptosis and some myosis on right side noticed on one occasion. Some distension of abdomen, with dyspeptic symptoms and occasional vomiting. Some frontal headache and disturbance of vision.

April 3.—Discharged; could walk feebly with a stick, but gait spastic.

June 8.—All four limbs weaker than in April. Left grasp weak; right very weak; some tremor now on effort to squeeze. Claw-hand on right side, slightly on left. Interossei wasted. Cannot separate fingers on right side; can do so feebly on left side. Cannot touch tip of nose accurately with either index when eyes closed. Dorsiflexion of right ankle still absent, of left weak. Gait feeble and spastic. Plantar reflex generally absent, but extensor response obtained once. No ankle clonus now. Knee-jerks much less exaggerated. Sensation to pain impaired and numb over both lower limbs and up to umbilicus in front and to iliac crests and upper sacrum behind; also on radial border of right upper limb and over the first four digits; loss of temperature sense over the same areas. Touch can be felt except over the soles. Over the trunk tactile sensation is less acute, pain sensation less acute on the right side than on left. Electrical reactions normal.

Distinct ptosis and myosis on right side (variable). Visual fields apparently normal, but in the outer half of the right visual field a finger seems to him to "shake."

Case 2.—Hysterical contracture of twelve years' duration, rapidly improving under treatment.

(IV.) Dr. LEONARD GUTHRIE.—*A mild case of Thomsen's disease.*

Boy, aged 11. Duration of symptoms twelve months. Metacarpal bones of both thumbs adducted, first and second phalanges extended and fingers flexed at metacarpo-phalangeal joints. First joints extended, terminals flexed. On grasping an object could not let go easily. The upper limbs became temporarily rigid on voluntary movement after a period of rest, but the rigidity speedily passed off when a few active movements had taken place. Similar temporary rigidity affected the lower limbs, but was only noticeable after rest. He complained that his legs felt stiff on starting to walk. The position of the hands was constant, even during sleep. It somewhat resembled that of tetany. The boy was intelligent and not neurotic. There was no family history of Thomsen's disease.

(V.) Dr. Newton Pitt.

(1) *Case of insular sclerosis.*—Wm. T., aged 20. Liable to periodic bilious attacks. Since June, 1899, he noticed he could not read small print on account of the constant oscillation of his eyeballs. In October anæsthesia with analgesia up to the groins suddenly developed, and three times within a week he was sent home as intoxicated on account of his ataxic gait. His legs tired readily and were rather stiff. When seen in October, 1899, he had an unsteady, feeble, slightly spastic gait which soon improved considerably. The area of anæsthesia also diminished and finally disappeared. The knee-jerks were exaggerated and there was an extensor plantar reflex. There was partial optic atrophy, especially in the outer part of the discs, and more marked in the right eye, vision $\frac{6}{60}$. No ocular paralysis. Slight constant tremors of head when unsupported. Speech slightly monotonous but hardly scanning.

(2) Ed. A., aged 40. Eighteen months ago anæsthesia of second division of right fifth cranial nerve. Thirteen months ago, after an attack of gout, his gait became very unsteady, the right leg was weaker than the left. When tired he has noticed he sometimes has had diplopia with the image displaced laterally. When seen in January, 1900, no diplopia, optic discs, fields of vision, pupils and speech normal. He is so unsteady in his gait, which is also somewhat spastic, that he moves about with great difficulty. The right grasp is weaker than the left and he could not touch his nose when his eyes were shut; this has gradually improved. In bed his legs not infrequently twitch involuntarily. There is pain in the lumbar and sacral region. No bladder nor rectal trouble. Very brisk knee-jerks with extensor plantar reflex. Clonus often comes on when he attempts to walk, but with physostigma this diminished and his gait has become less spastic. During the past five months no marked changes have taken place.

(*Additional note, June* 21, 1900.)

He still has occasional diplopia, due to weakness of the right external rectus. There is now some early optic atrophy in the right disc on the outer part, and possibly some in the left eye. His vision is rather defective, he has slight hypermetropic astigmatism, but even when this is corrected his vision is about $\frac{6}{9}$. He had numbness in the right thumb for two months, so that he was unable to button his coat; this has now passed off. The diagnosis appears to lie between insular sclerosis and combined paraplegia.

(3) Nicholas R., aged 37. Five years ago he had numbness of his fingers with a squint which lasted for a month. In January, 1900, pain in sacrum, which has continued, numbness in legs, thighs, and fingers. In March his gait became unsteady and has continued to get worse. He staggers in his gait, throws up his legs erratically, especially the left, but there is some spasticity. Knee-jerks increased. Speech slovenly and tremulous. When seen in April he had numbness with anæsthesia of fingers, especially of left hand; this has now passed off. Extensor plantar reflex, but feeble in right side. He in April was unable to touch his nose with his right hand with his eyes shut; this defect has passed off. At the onset of the attack retention of urine. Paralysis of right external rectus which has greatly diminished now. Optic discs in April normal. Right pupil smaller than left; reactions normal. Slight chronic glaucoma. The defect in walking increased rapidly at first, but since April has not varied much. The anæsthesia of hands has greatly decreased.

(*Additional note, June* 21, 1900.)

The discs appear to be whiter than in the spring, and suggest an early condition of optic atrophy, but this is still indefinite. His vision is not up to the normal. The weakness of the right external rectus is much less, but there is still diplopia. The right field of vision is contracted laterally. The pupils are equal, and the tension of the eyes is normal.

BRAIN.

PART III., 1900.

Original Articles and Clinical Cases.

THE PATHOLOGY OF HERPES ZOSTER AND ITS BEARING ON SENSORY LOCALISATION.

BY HENRY HEAD, M.D., F.R.S.

Assistant Physician to the London Hospital,

AND

A. W. CAMPBELL, M.D.

Pathologist to the County Asylum, Rainhill.

From the Laboratory of the London County Council, Claybury, and the Laboratory of the County Asylum, Rainhill.

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18 and 19.—Cases of Zoster in which the Gasserian Ganglion was affected.
20 and 21.—Cases of Zoster in which no changes were found after death.

Our best thanks are due to Dr. Pye-Smith, Dr. Hale White, and Dr. Perry, of Guy's Hospital, for their kindness in permitting us to use their cases; to Mr. Lunn, the Superintendent of the St. Marylebone Infirmary, for placing the whole of his material at the service of one of us; to Dr. Wiglesworth for the use of the cases from Rainhill, and to Dr. Jones for the use of the Claybury cases.

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INTRODUCTION.

It would be useless to attempt a review of all the literature that has grown up around the subject of "Herpes Zoster," for from 1895 to the present time alone over seventy papers have been written on this subject, very few of which have any bearing on the matter of the present communication.

Moreover, our work deals with herpes zoster from two aspects. Firstly, we have determined the pathological lesion which underlies this disease, and, secondly, we have attempted thereby to determine the cutaneous distribution of certain fibres that enter each posterior root ganglion. We shall, therefore, only allude to such communications as throw light on the pathological lesions in herpes zoster, or on the distribution of the fibres which enter the posterior root ganglia.

It was not until the appearance of von Bärensprung's classical paper (23) in 1861 that herpes zoster was stated to be definitely of nervous origin; and when von Bärensprung crowned his long series of admirably reported observations by a *post-mortem* examination (1), its association with a lesion of the posterior root ganglion was universally accepted. But as his conclusions in their passage from book to book have undergone modification, and as the position of the question he set himself to answer has been widened by our increased knowledge of the structure of the nervous system, it will be well to consider this first successful *post-mortem* examination more carefully. Moreover, we must remember that although von Bärensprung rightly placed the position of the lesion in the posterior root ganglion, he thought this structure stood in no connection with the fibres of the posterior root or peripheral nerve, but had special nerve-fibres of its own.

The eruption seems to have occupied the area we have called dorsal 7; for it ran in the form of a girdle over 2 inches in breadth between the 6th and the 9th ribs, passing the middle line behind for one or two lines at the level of the 5th to the 8th spines, to end beneath the xyphoid process. Death followed from tuberculosis forty days after the first appearance of the eruption.

The spinal cord and both anterior and posterior roots were stated to have been normal; but "Nachdem die Intervertebralkanäle geöffnet und die Intercostalnerven vom 5ten bis zum 9ten freigelegt waren fiel sogleich eine grössere Dicke und vermehrte Röthung des 6ten, 7ten und 8ten am meisten aber des 7ten auf, die von einer Anschwellung des mit erweiterten stark geschlängelten Gefässen durchzogenen Neurilems vorzugsweise abzuhängen schien. Der Durchmesser des 7ten Nerve übertraf fast um die Hälfte den des 5ten und des 9ten Intercostalnerven . . . . Den 6ten und 8ten Nerv zeigten die nämliche Röthung und Anschwellung aber etwas weniger stark und auf eine kürzere Erstreckung als den des 7ten." He then states that he found the remains of extravasated blood in the ganglion, without mentioning to which of the three ganglia he alludes.

This case seems to have borne a close resemblance to No. 2 and No. 4 of our series, in both of which cases the swelling of the affected ganglion and nerve was obvious to the naked eye. Thus by little more than a naked-eye examination von Bärensprung was enabled to prove that the ganglion was affected in herpes zoster.

The next report of a *post-mortem* examination was made by Charcot and Cotard in 1865 (4). A woman suffering from cancer of the breast developed zoster over what appears to have been the 3rd and 4th cervical areas. At the autopsy secondary growths were found to have invaded many of the vertebræ, especially in the cervical region. The 4th cervical vertebra was found to be profoundly affected. The only change found in the nervous system consisted in an active injection of the capillaries of the ganglia and nerves, a "véritable neuritis" without concomitant alteration of the ganglion cells or nerve-tubes.

This case is so poorly reported that even from the point of view of a naked-eye examination it is valueless, either to elucidate the pathology or localisation of the lesion of herpes zoster. It would seem to have closely resembled case 14 of our series, where examination, even by the simple methods of that day, would have revealed marked changes in the affected ganglion.

The next case was reported by Weidner in 1870 (18). In a paper on three cases of zoster he reported two autopsies with negative results. This is not surprising, since in his first case, although the eruption lay over what we have called cervical 4, he only examined the cord ganglia and nerves between cervical 7 and dorsal 2; and in his second case the patient died five years after the eruption.

In the same year E. Wagner (17) reported the result of an autopsy on a tuberculous patient who had developed an attack of zoster over the 9th and 10th ribs seven days before death. The six lower dorsal and the 1st and 2nd lumbar vertebræ were laid bare by tubercular caries, and the dura mater was lined with a thick layer of cheesy pus. Only the ganglia were examined microscopically, and the 9th, 10th, and 11th dorsal were said to have been affected. But it is obvious that an incomplete examination of so complicated a case could add little to the knowledge of either pathology or localisation.

In 1871, Oscar Wyss (19) reported a case of zoster of the whole first division of the trigeminal nerve, where death occurred seven days after the appearance of the eruption. The ophthalmic vein was thrombosed and the eye-muscles contained small abscesses, and the connective tissue of the eyeball was infiltrated with pus. From the point where the first or ophthalmic division leaves the Gasserian ganglion to enter the eyeball it was surrounded by extravasated blood. The second and third divisions were unaffected; but attached to the inner side of the Gasserian ganglion lay a red mass 1 cm. broad, apparently consisting of extravasated blood. Microscopically, there was an extravasation of blood into the inner aspect of the ganglion and into the first division of the trigeminal nerve. There is also said to have been "purulent inflammation" of the ganglion, pushing the ganglion cells apart.

In 1875, Sattler (16) also reported a case of herpes ophthalmicus, extremely well worked out according to the methods then known. A man of 85 was poisoned by carbonic oxide gas. Four days later neuralgia came on over the right half of the forehead, and in a few days the forehead, the side of the nose, and the eyelids, became covered with an eruption of herpes zoster. Death occurred fourteen days afterwards. The Gasserian ganglion was found to be infiltrated with small round cells, and there was marked destruction of the ganglion cells. The ophthalmic division of the nerve was degenerated. The other two divisions were normal.

By this time it had come to be recognised that the ganglion was affected in cases of zoster, and in 1876 Kaposi (10) reported a case in which he arrived at a very odd result. A man of 54 died seven days after the appearance of an eruption that had the following distribution: "Auf der allgemeinen Decke des Unterleibes rechts über den Darmbeinkamm und mit diesem parallel laufend eine continuirliche Folge von Herpes-gruppen welche etwa 1½ bis etwa 1 Zoll vor und über der Symphyse sich erstrecken." The area affected seems to have corresponded with our dorsal 11. But he only examined the ganglia of dorsal 12 and lumbar 1 to 5, and states that hæmorrhages were present in the periganglionic fat of dorsal 12, lumbar 1, 2 and 3, and that the protoplasm of lumbar 2, the most affected ganglion, was pale and retracted. In the light of our present knowledge it is impossible that these changes could have been associated directly with the eruption over the area he describes.

In his text-book Kaposi again alludes to this case, and states that he also examined a case of herpes frontalis and found hæmorrhage and destruction in the Gasserian ganglion. We have not, however, been able to find any further account of this second case, and the first case, though frequently quoted, is valueless as a contribution to the pathology of herpes zoster.

In 1879, Chaudelux (3) reported the case of a woman who died of phthisis many months after an attack of zoster. He says the remains of the eruption lay over the 2nd and 3rd intercostal spaces on the left side, but gives no further details of its distribution. The 2nd and 3rd dorsal ganglia of the left side are said to have been double the normal size, and certain zones in these ganglia were completely transformed, ganglion cells and nerve-tubes were destroyed, and their place taken by dense connective tissue. From the figure he gives he evidently saw the condition figured by us on plate 1, fig. 2B. The spinal cord was destroyed in extraction, and the nerves, having been hardened in alcohol, gave no positive result.

In 1881, Lesser (12) published the first two satisfactory *post-mortem* examinations of cases of zoster of the trunk, and followed up his first communication by a second in 1883 (13), in which he reported a third case. In the first of these three cases the eruption lay over the right side of the neck, bounded in front and behind by the middle line, above by the lower jaw, and below by a line passing round the shoulder roughly to join the spine of the 2nd dorsal vertebra behind, with the third costal cartilage in front. This lower border dipped in front to occupy the extreme upper part of the anterior surface of the right arm. Death occurred twenty-six days after the eruption first appeared. The 4th cervical ganglion of the right side contained a focus visible to the naked eye, and situated on that side of the ganglion opposed to the anterior root. Microscopically, this focus consisted of a mass of cells surrounding what appeared to be the remains of a hæmorrhage. The remaining ganglia, the posterior roots, the nerves, and the spinal cord were stated to be normal; but at that date no method existed by which the acute degenerative changes that probably existed could have been demonstrated.

In Lesser's second case the eruption appears to have occupied the area that we should call dorsal 8, and death took place about nine days after its first appearance. To the naked eye the 8th dorsal ganglion was very red, but not swollen. On microscopical examination this reddened area was seen to consist of a hæmorrhage containing broken-down ganglion cells, and surrounded by a mass of inflammatory tissue. The case seems closely to have resembled Nos. 2, 4, and 5 of our series. Lesser thought that there was a similar though less pronounced change in the 9th dorsal ganglion, but he carefully states that there was no hæmorrhage or breaking-down of nerve elements, and our experience leads us to suspect that he was mislead by the hyperæmia not infrequently present in normal ganglia; for he was evidently unwilling to believe that one ganglion could supply the whole of the area occupied by the eruption. The other ganglia, peripheral nerves, and spinal cord showed no change. Admirable figures accompany this paper, which is the first serious contribution to the pathology and localisation of zoster of the trunk.

Lesser's third case (13) died three weeks after an eruption that lay over the mamma and occupied the area we have called dorsal 5. On microscopical examination the 5th dorsal ganglion was found to be markedly altered. The nervous elements of the upper half of the ganglion were replaced by connective tissue, and the sheath of the ganglion over this area was thickened. The peripheral nerve of this ganglion also showed changes, for the normal fibres were in places widely separated by fields of granular tissue. He states that the 4th ganglion also was altered, but that the 4th nerve was normal. As, however, he gives no figures in this paper, it is difficult to gather the extent of these changes, and he admits that the 4th ganglion was not so carefully examined as the 5th.

In 1883, Pitres and Vaillard (15) reported the *post-mortem* on a curious case. After mentioning a number of cases in which they had examined the nerves in the neighbourhood of bed-sores, they mention a case in which there were scars of zoster in the 6th intercostal space on the right side, and an eruption that they thought was zoster in the 11th intercostal space of the same side. On microscopical examination they state that in the 6th dorsal ganglion nerve-fibres were destroyed but the cells were perfect, that there was parenchymatous degeneration and some sclerosis of the 6th dorsal peripheral nerve and degeneration of the posterior roots of the 6th dorsal. They also state that the 11th dorsal peripheral nerve was degenerated and sclerosed, but that the ganglion and roots were normal. The cord was everywhere normal. In the light of subsequent experience it would seem that the scars in the 6th intercostal space were probably due to an old zoster, but that the eruption in the 11th space cannot be classed under the heading of true zoster. However, the case is so poorly reported that it can add but little to our knowledge.

In 1884, Curschmann and Eisenlohr (5) published two cases in which an eruption of zoster was followed by the development of small nodular swellings on the peripheral nerves. In the first case several of these swellings were removed by operation. Microscopically they were found to consist of healthy nerve-fibres surrounded by small hæmorrhages, exudation of inflammatory cells and engorged cappillaries, in fact, a condition of "perineuritis acuta nodosa." This case died a year and nine months afterwards, and they found no change in nerves, ganglia, or cervical cord.

They also report a third case in which zoster appeared two days before death over the 11th rib and last intercostal space. On *post-mortem* examination the back muscles on the same side as the eruption were found to be infiltrated with blood, and through this infiltration passed the branches of the 10th and 11th dorsal nerves. The nerve-fibres in these branches were, however, unaltered, and the 10th, 11th and 12th dorsal ganglia and the dorsal and lumbar cord were normal. But it is not improbable that these observers, like Pitres and Vaillard, were misled by their idea that zoster was due to changes in the peripheral nerves. Thus the fact that the anterior divisions of the 10th and 11th dorsal nerves passed through the broken-down muscles, caused them to imagine that these nerves must have been the seat of the lesion in spite of the fact that their peripheral branches do not supply the area over which the eruption lay (*vide* our plate 17). Probably the seat of the lesion in this case was the 9th dorsal ganglion, which they neglected to examine.

In 1884, Dubler (7) published the results of an examination of two cases. Of these we will consider the second and more straightforward case first. The distribution of the eruption, which occurred 103 days before death, was as follows:—"Rechts über den unteren Rippen und über der unteren Bauchgegend eine von oben hinten nach vorn unten verlaufende 5 cm. breite gürtelförmige Hautpartie . . . . . Diese Hautveränderung beginnt hinten an der Wirbelsaüle, reicht vorn bis zur Mittellinie wo sie 4 Querfinger oberhalb der Symphyse endet. Seitlich bleibt sie 3 Querfinger von der Spina Anterior Superior entfernt."

Microscopically the spinal cord was normal. The 9th dorsal ganglion showed interstitial changes, degeneration of nerve-bundles and small pin-point hæmorrhages and dots.

The 8th and 10th dorsal ganglia were normal. The 9th intercostal nerve and 9th dorsal roots were degenerated, and there was a small amount of degeneration in the 10th intercostal nerve.

Dubler's first case is less clear owing to the fact that the patient had tubercular necrosis of several ribs. The eruption seems to have occupied the area we have called the 8th dorsal, and the patient died 144 days after its first appearance. On the 7th, 8th and 9th ribs were caseous masses, due to necrosis of the bone. The 6th, 7th, 8th and 9th intercostal nerves passed through these swellings. A few nerve-fibres were degenerated in the anterior division of the 7th intercostal nerve; there was marked degeneration in the posterior and anterior primary divisions of the 8th intercostal nerve, and slighter degeneration in the anterior division of the 9th intercostal. Ganglia, cord and posterior roots were said to be normal at the level of the 6th, 7th, 8th and 9th dorsal.

In 1887, Leudet (14) published a somewhat superficial paper in which he mentions a case of herpes frontalis where he found an old inflammatory process in the frontal nerve, and a degenerative condition of the Gasserian ganglion.

Thus up till the time we began to investigate the pathology of herpes zoster there had been two well reported autopsies on cases of zoster ophthalmicus [Sattler (16), Wyss (19)], and five satisfactory reports on zoster of the trunk [Lesser, three excellent cases (12 and 13), Chandelux, one fairly reported case (3), Dubler, one excellently reported case (7)].

To these we now add twenty-one cases at all stages after the eruption.

PART I.—THE PATHOLOGY OF ZOSTER.

Chapter 1.—Changes in the ganglion of the Posterior Root.

If the patient has died with the eruption still out upon his skin the affected ganglion will be found to be in a condition of profound inflammation. The interstitial tissue will be crowded with small round cells which stain deeply with methylene blue and other nuclear dyes. Here and there these inflammatory cells may be closely massed into clumps, and such foci may be scattered round the periphery and in the central tissue of the ganglion.

If these foci of inflammatory cells are examined in serial sections they will occasionally be found to be situated around extravasated blood which has undergone more or less change according to the length of time at which death has occurred after the first appearance of the eruption.

But not infrequently the hæmorrhage is of much greater extent and produces changes that are noticeable without the aid of the microscope.

In Case 1, where the patient died only three days after the outbreak of the eruption, the whole centre of the ganglion is ploughed up by a large hæmorrhage, and this condition produced an alteration in consistence that attracted attention as soon as the ganglion was fixed. In both Case 2 and Case 5 a swollen condition of the peripheral nerve close to the ganglion was noticeable at the autopsy. Thus the intensity of the inflammation in the interstitial tissue of the ganglion is such that blood is extravasated, it may be only as a microscopic hæmorrhage or it may be in sufficient quantity to produce an actual swelling of the affected part.

The inflammation and hæmorrhage are situated in the dorsal aspect of the ganglion, *i.e.*, in that portion opposed to the anterior root. The ganglionic substance may be destroyed to a greater or less extent, but if hæmorrhage has occurred at all we have always found it in the dorsal half of the ganglion.

In the centre of these hæmorrhagic foci the ganglion cells are absolutely destroyed. But in the surrounding zone of small round cells the remains of ganglion cells can be generally seen in the form of pale masses, which do not stain with methylene blue, but stain strongly with safranin. Further, towards the periphery of these inflammatory foci some ganglion cells usually appear, when stained by Nissl's method, as dark blue lumps without any differentiation of structure.

In some cases the nuclei of the ganglion cells seem swollen and, by Nissl's method, stain of a uniform blue colour, which is so intense that no nucleolus and no trace of the normal reticular arrangement of the nucleus is recognisable. Such nuclei retain their colour so firmly that they are still well stained when all other structures have given up the dye. In van Gieson preparations these nuclei appear of a dark brown colour, and with Ehrlich's hæmatoxylin they assume a uniform deep purple.

The substance of the bodies of these cells has a uniform blurred appearance, entirely devoid of definite structure, and the chromophilic particles of Nissl are completely obscured.

Such are the changes found in the cells of the posterior root ganglion, starting from within the hæmorrhagic centre of an inflammatory focus and working outwards towards the periphery. The extent to which the cells show one or other of these changes varies in different cases.

But in the affected ganglia many cells are usually seen which show no noticeable alteration, and in no instance of spontaneous zoster have we been able to see those minor chromatolytic changes that are so commonly present in degenerative diseases of the nervous system. The inflamed ganglia show no ganglion cells with extruded or excentric nuclei with vacuolation or partial disappearance of Nissl's particles. Thus, where such conditions were present in addition to the herpetic lesion as in No. 15 (a case of fractured spine), or in No. 14 (a case of malignant disease), the contrast to the conditions usually seen in herpetic ganglia was most instructive.

Over that portion of the ganglion which is inflamed the sheath generally shows similar changes. The vessels are engorged and occasionally blood may be extravasated, but in all cases where the inflammation in the ganglion was severe the sheath was invaded by multitudes of small round deeply staining cells.

On account of the severity of these inflammatory changes in the ganglion it is difficult, even in the serial sections at our disposal, to select any individual artery to an interference with which the focal lesion can be ascribed. But in one acute case (No. 4) an arterial branch, entering at the distal pole of the ganglion and proceeding towards the lesion, differed from similar vessels in the normal part of the ganglion in that an abundance of extruded leucocytes occurred along its course. With lapse of time the identification of such an artery becomes increasingly impossible.

If not severe, the inflammation may pass away and leave no recognisable change behind in the ganglion. In Case 20, where the eruption was scanty and the inflammation of the skin not severe, no changes could be found 139 days after it first appeared.

But the greater the severity of the eruption, and the profounder the scarring it leaves behind it, the more certainly will permanent changes be found in the posterior root ganglion. Thus out of thirteen cases that were examined between 57 and 790 days after the eruption appeared, eleven showed obvious microscopical evidence of a past inflammation in the posterior root ganglion.

As soon as the virulence of the inflammation has expended itself absorption begins. Round cells are seen within the capsule of each dead ganglion-cell, apparently eroding it. In one case (No. 15) it seemed as if some of these scavenger cells might have been derived from the cells of the capsule of the ganglion cell itself.

The effused blood undergoes retrogressive changes, and if not completely removed remains only as a mass of brownish granular deposit in the centre of the scar tissue. (Cases 8, 18 and 19). For ultimately the focus of inflammation becomes converted into fibrous tissue, and the density and extent of this scar depends on the severity and extent of the original inflammation. Usually the final result is a scar occupying from one-sixth to a half of the ganglion. Within this area all ganglion cells and nerve-fibres are destroyed, and no structure remains to show where they once existed. But in several cases a few healthy ganglion cells, and still more often a few healthy nerve-fibres, can be seen scattered in the scar tissue.

Over this scar in the ganglionic tissue, the sheath is thickened and altered in appearance (plate 1, fig. 2B, plate 6, fig. 2). The sheath of a normal ganglion is made up of crescentric layers of fibrous tissue separated from one another by lymph spaces, and presents on section somewhat the appearance of the sheath of an onion. Over the sclerosed patch in the ganglion this appearance is lost, and the sheath becomes converted into an almost homogeneous mass of dense fibrous tissue. The sheath may become three times the thickness of the normal, and present a curious non-lamellated appearance, in marked contrast to the normal wavy appearance of the remainder of the sheath.

The sclerotic changes in the ganglion and its sheath are well shown on plate 1, fig. 2B, which represents the affected ganglion in a case that died 153 days after the eruption came out. The affected portion of the ganglion stains a brilliant red colour with van Gieson's picro-hæmatoxylin method in marked contrast to the purple red colour of the ganglion of the opposite side (plate 1, fig. 2A), which contained its normal complement of nerve-cells and fibres.

Now such a condition obviously corresponds to what might have been expected to result from an acute condition, such as that shown on plate 1, fig. 1.

Thus, in conclusion, the acute changes found in the ganglion in a case of herpes zoster consist of an (1) Extremely acute inflammation with the exudation of small round deeply-staining cells; (2) Extravasation of blood; (3) destruction of ganglion cells and fibres; (4) inflammation of the sheath of the ganglion.

If severe such a condition ultimately leaves a scar in that part of the ganglion affected and leads to thickening of the sheath above the affected area. On the other hand if the eruption has not been severe all traces of the inflammation present in the acute stage may pass away, leaving the ganglion apparently normal.

Chapter 2.—Changes in the Posterior Nerve-Roots.

It is obvious that with so considerable a destruction in the posterior root ganglion secondary degeneration must occur in the posterior nerve-root to an equivalent extent. In fact we are here dealing with a lesion as strictly localised as that of any experiment.

Moreover, as death occurred at the most varied intervals after the outbreak of the disease, we had the opportunity of learning the length of time that is required for a nerve-root to degenerate after partial destruction of the ganglion.

In Case 2 death occurred eight days after the first appearance of the eruption, and here no change could be found in the posterior roots on careful examination by Marchi's osmium bichromate method.

Thirteen days after the eruption first appeared in Case 4, profound degeneration was present in the posterior roots, and it is probable that this degeneration begins to make its appearance ten days after the appearance of the eruption. For although the posterior roots could not be examined in Case 3, the degeneration in the root after it had entered the spinal cord was so profound that it was probably degenerated in its extraspinal course. This case died on the eleventh day after the eruption began to appear.

This degeneration is of the usual acute type, and by Marchi's method is seen to consist of a profound disintegration of the myelin sheath. The broken-down sheath stains deep black, and black dots can be seen lying in rows like broken beads within the primitive sheath (plate 16, fig. 1).

In the earlier cases fibres are also seen in which the normal cylinder of medullated substance has been replaced by collections of black or dark brown globules. The groundwork of the medullary sheath of these fibres stains of a pale gray colour, and in it are distributed crowds of coarse refractile dark brown granules, which occasionally occur in lines or fusiform clumps. These fibres, swollen in some places and contracted in others, have a wavy outline.

This acute change seems to have reached its height by about the fifteenth day after the appearance of the eruption. The products of acute degeneration are then gradually cleared away, and if the destruction has been profound, fibrous tissue takes the place of the destroyed nerve-fibres. If, however, the degeneration has not been of considerable extent, this disappearance of the products of acute destruction may produce no recognisable change in the posterior root.

However, the extent of the acute lesion is usually sufficiently great to cause a noticeable increase of connective tissue in one or more bundles of the posterior root.

Thus fifty-seven days after the eruption this secondary sclerosis was already quite evident (Case 6), but one hundred and fifty-three days after the eruption (Case 9) the last remains of the products of acute degeneration could still be seen amongst the secondary fibrous tissue. After two hundred and seventy-two days (Case 10), all signs of acute degeneration had disappeared, but the sclerosis was well marked, more than one half the posterior root being replaced by fibrous tissue.

If the lesion has been severe the fibrous tissue becomes less vascular and finally settles down into permanent scar tissue, clearly visible seven hundred and ninety days after the eruption (Case 13).

Thus the changes we have found in the posterior nerve-root corresponded to the results that might have been expected from the lesion of the ganglion. They consisted of an acute degeneration followed by a greater or less amount of secondary sclerosis according to the severity of the acute destruction.

The anterior root was in all cases normal.

Chapter 3.—*Changes in the Peripheral Nerves.*

As might have been expected a lesion of the ganglion such as we have described produces marked secondary degenerative changes in the fibres that enter the posterior root ganglion. In the mixed trunks of the peripheral nerve close to the ganglion these acutely degenerated fibres stand out clearly (when stained by Marchi's method), against the normal fibres of the anterior root. The number of these degenerated fibres varies considerably with the severity of the ganglionic lesion. It is best studied in the simpler trunks of the mid-dorsal region rather than in the more complicated anastomoses of the cervical and upper lumbar regions.

Eight days after the eruption (Case 2) no acute degeneration could be found in the peripheral nerves in connection with the affected ganglion, but thirteen days after (Case 4) degeneration was present to a marked degree.

By Marchi's method the degenerated fibres show the same breaking up of the myelin sheath and irregularity of outline already described when considering the changes in the posterior roots, appearances identical with those seen after an experimental lesion.

Both posterior primary and anterior primary divisions are markedly affected, but the number of degenerated fibres in the posterior primary division always appears to be greater, probably owing to the almost entirely afferent nature of this branch in the dorsal region.

This degeneration can be traced right back to the fine twigs which pass upwards into the skin to supply the area over which the eruption is distributed.

With time the products of degeneration are removed from the peripheral nerve, and if the ganglionic lesion is not severe it may be impossible to be certain of any abnormality in the peripheral nerves. On the other hand, if the lesion has been a severe one the nerve-fibres that have degenerated are replaced by fibrous tissue and whole bundles of the nerve may be sclerosed (plate 16, fig. 3).

This sclerosis was evident in Case 18 thirty days after the eruption but, on the other hand, Marchi's method still showed some remains of acutely degenerated fibres 100 days after the eruption alongside the sclerosis (Case 8). The sclerotic change, once established, is permanent, and was visible 790 days after the eruption (Case 13).

Thus, in the peripheral nerves degeneration seems to appear, to disappear and to be replaced by sclerotic changes at the same periods after the initial lesion in the ganglion, as was the case with the posterior roots.

So far we have treated the peripheral nerves as if they were not affected by any condition other than that of degeneration secondary to the ganglionic lesion. But in two of our cases hæmorrhage and inflammation occurred not only in the ganglion, but in the peripheral nerve in connection with it. In Case 2 this hæmorrhage extended for about 1 cm. down the course of the combined peripheral trunk, which was swollen until its diameter was that of a normal ganglion (*vide* also Case 4, plate 8, figs. 3 and 4).

Chapter 4.—Degeneration in the Spinal Cord.

When a posterior root ganglion is excised, or a posterior root divided experimentally, acute degeneration takes place in those fibres which, entering the spinal cord by that root, run upwards in the posterior columns. Thus it is not surprising that such lesions of the ganglion as we have described in the previous section should be attended by acute degeneration of the root-fibres in the posterior columns of the spinal cord.

This degeneration probably appears about the ninth or tenth day after the eruption. For in Case 2, although the ganglionic lesion was an extremely severe one, no degeneration had made its appearance in the spinal cord eight days after the eruption. On the other hand, in Case 3 acute degeneration was present to a marked degree eleven days after the first appearance of the eruption. Thirteen (Case 4) and fourteen days (Case 5) after the eruption first appeared this degeneration was extremely well marked and appeared to have almost reached its full development.

When dealing with the similar degeneration in the fibres of the posterior roots we drew attention to the rapidity with which the products of this acute degeneration were removed and replaced by secondary fibrous tissue. In the spinal cord, on the other hand, the products of acute degeneration are removed much more slowly. Thus, fifty-seven days after the eruption in Case 6, the products of degeneration in the posterior roots showed signs of absorption, and these roots were already considerably sclerosed. But the degeneration in the spinal cord was extremely well marked and the degenerative material that stains black with osmic acid showed no signs of absorption. In the same way in Case 18 the products of degeneration in the root of the Gasserian ganglion showed marked absorption, with the deposition of secondary fibrous tissue, thirty days only after the outbreak of the eruption. Yet the degeneration in the medullary or descending root of the 5th nerve was profoundly marked and showed no signs of absorption.

One hundred and fifty-three days after the eruption (Case 9) the acute degeneration in the spinal cord was still profoundly marked, but in 272 days it had disappeared.

Unfortunately we possess no case between 153 and 272 days after the eruption, and cannot therefore say the earliest date at which the acute degeneration is cleared away; for in Case 9 the degeneration showed no signs of diminution, and in Case 10 it had gone. But in Case 19, where the eruption lay over the ophthalmic division of the trigeminal, no signs of acute degeneration could be found in the pons or medulla 190 days after the eruption first appeared. This case is, however, open to the objection that the scarring was slight and the lesion in the ganglion not severe.

When the degeneration is cleared away from the spinal cord it leaves no perceptible sclerosis behind it, probably owing to the relatively small number of fibres destroyed. Thus, 272 (Case 10), 481 (Case 11), 515 (Case 12), and 790 (Case 13) days after the eruption no abnormal changes of any kind could be found in the spinal cord that could be referred to the herpetic lesion.

The course followed by the degenerated fibres in the spinal cord is exactly that which might have been expected from the known results of experimental division of posterior roots. Where the pencils of the degenerated posterior root penetrate the spinal cord there is a brief length where there is no marked blackening of the fibres. For, as Obersteiner has shown, the medullary envelope of each fibre is here reduced to small proportions. But centralwards of this point degenerated fibres can be seen in a transverse section running for a short distance along the inner margin of the tip of the posterior cornu. This field of degeneration hugs the posterior horn, and the degenerated fibres are most numerous opposite the substantia gelatinosa Rolandi.

Thence the field tapers inwards, to end about two-thirds of the way along the posterior horn.

In the centre of the gray substance of the posterior horn, immediately ventral to the substantia gelatinosa, a few degenerated fibres are usually seen cut transversely and apparently of small calibre.

In longitudinal sections pencils of degenerated fibres can be seen streaming inwards to join a mass of degeneration that ascends the cord in the root zone of the posterior column (plate 15, figs. 1 and 2). This stream of degeneration contains fibres of both small and large calibre.

One segment below the entry of the diseased root a few fibres can be seen cut transversely and scattered irregularly in the root zone close to the posterior horn. These descending collaterals are fewer in number than we expected, so few in fact that they must be looked for carefully in order to be seen at all. Two segments below the entry of the diseased root we have also seen a few scattered degenerated fibres, but sometimes we have not been able to be certain of any degenerated fibres at this level.

Tracing the field of degeneration upwards we find that one segment above the entry of the degenerated root the blackened fibres lie entirely in the root-zone of the posterior column, and the posterior horn is clear of degeneration. The subsequent destination of the field of degenerated fibres varies according to the position of the affected ganglion.

In Case 7 where the 2nd dorsal ganglion was affected and the eruption lay over the inner aspect of the arm, the degenerated fibres in the spinal cord can be clearly followed up to the inner portion of the nucleus cuneatus in the medulla. At the level of the 1st dorsal root they lie on the inner aspect of and apparently in direct contact with the posterior horn. At the level of the 8th cervical they are separated from the horn by a thin band of normal fibres. At the level of the 6th cervical they form a tiny triangle with its base on the external (dorsal) surface of the postero-external column and its inner side in close opposition to the inter-columnar septum. In this position they can be followed up the spinal cord, gradually decreasing in number, but a remnant can be clearly traced into the inner portion of the nucleus of the funiculus cuneatus (plate 10, fig. 1).

We have examined no case in which the eruption was situated entirely over the leg. But in two of our cases (No. 4 and No. 8) the eruption lay over the area of the 12th dorsal, the highest to send branches to the front of the thigh. Fortunately one of these cases (No. 4) is an early (13 days), the other (No. 8) a late (100 days) example (plate 12, figs. 1 and 2).

At the level of the 10th dorsal root two segments above the entry of the diseased fibres, the degeneration forms a strip separated by a distinct interval from the posterior horn, reaching internally to a point almost opposite Clarke's column. In the central portion of this strip the fibres are more closely packed than in the outer portion. Higher up, at the level of dorsal 9, the degenerated fibres have shifted further inwards towards the middle line and are mainly situated in the inner half of the postero-external column. This strip begins in the neighbourhood of Clarke's column and extends as before to the periphery, but the degenerated fibres are still more closely packed in that part nearer the central portion of the cord. Two segments higher (dorsal 7) a small number of the fibres of this strip lie in the outer portion of the postero-internal column (Goll). Thus as they ascend the cord the degenerated fibres are gradually pushed inwards, diminishing in number on their upward journey. At the level of dorsal 6 (Case 8), 150 degenerated fibres were counted as opposed to 210 at the entry of the affected root. At the level of dorsal 3 the strip of degenerated fibres lies on the inner side of the boundary separating the postero-internal from the postero-external columns. At the level of cervical 7 the central half of this strip lies against the postero-median septum, whilst that half nearer the peripheral portion of the cord lies along the outer border of the postero-external column. In Case 8 the degeneration cannot be followed higher than this level, but in Case 4 a few degenerated fibres can be seen two segments higher (cervical 5).

Thus in a suitable case, where the area of the eruption extends on to the arm, the degenerated fibres can be followed in the cord from the root zone to the postero-external column, and by this path up to the nucleus of this column, the nucleus cuneatus. Where, on the other hand, the eruption lies on the leg, the field of degeneration passes into the postero-internal column, and one half of the field finally lies against the posterior median septum. As the two cases we have examined were both instances of dorsal 12, the highest area that touches the leg, the more peripheral portion of the degenerated field is seen to lie at the juncture of the postero-internal and postero-external columns.

So far the degeneration we have observed in the spinal cord, secondary to the herpetic lesion of the ganglion, exactly confirms the results of experiments on animals. For the postero-internal column (Goll) in the cervical region, has been shown experimentally to consist almost exclusively of fibres from the leg, the postero-internal (Burdach) of fibres from the arm. But when the lesion lies in a ganglion of the dorsal region, between the 3rd and the 11th dorsal, this secondary degeneration in the spinal cord follows a somewhat different course.

This difference in behaviour is exemplified in Case 9. The degenerated fibres are seen to enter at the 7th dorsal root, and one segment above occupy the root zone adjacent to the posterior horn. They diminish in number on their upward course, and come more towards the periphery of the spinal cord, to disappear entirely at the level of the 1st dorsal. In the same way the degenerated fibres that enter at the 6th dorsal root in Case 3, disappear at the level of the 1st dorsal.

Thus, whereas a lesion at the level of the 12th dorsal will produce a degeneration which ascends fourteen segments, a lesion at the level of the 7th dorsal will cause degeneration, which ascends only five segments. This cannot be due to the length of time that has elapsed, for in thirteen days (Case 4) a lesion of the 12th dorsal ganglion had caused degeneration that ascended to the level of the 5th cervical, whilst in fourteen days (Case 5) a lesion of the

6th dorsal ganglion produced degeneration that ceased at the level of the 1st dorsal.

The following table illustrates this difference between the behaviour of the root fibres in the dorsal as opposed to the limb areas :—

	Lesion.	Highest Level of Secondary Degeneration.	Number of Segments.	Duration.
Case 7 ..	Dorsal 2	Nucleus Cuneatus ..	10	96 days.
Case 3 ..	Dorsal 6	Dorsal 1	6	14 days.
Case 9 ..	Dorsal 7	Dorsal 1	7	153 days.
Case 5 ..	Dorsal 11	Dorsal 6	6	14 days.
Case 8 ..	Dorsal 12	Cervical 7	14	100 days.
Case 4 ..	Dorsal 12	Cervical 5	16	13 days.

This difference of behaviour shows that the posterior roots in the dorsal region containing as they do afferent fibres from the trunk, consist mainly of short fibres which do not form a part of either the postero-internal or the postero-external columns in the cervical region of the spinal cord, whilst the long fibres that form these columns come almost exclusively from the leg and the arm respectively.

This fact with regard to the constitution of the roots in the dorsal region seems to have escaped experimenters, and is of interest in conjunction with the observations of Münzer (36), who found that division of the postero-internal and postero-external columns in the cord caused no loss of conduction of pain stimuli, but that destruction of the root zones when the postero-external and internal columns remained intact, abolished the conduction of painful impressions.

Chapter 5.—Zoster of the Trigeminal.

We pointed out in the Introduction that the first satisfactory report on the *post-mortem* appearances in zoster was given by Sattler (16) on a case of so called herpes ophthalmicus. He found an inflammatory lesion with hæmorrhages destroying both the nerve-cells and fibres of the Gasserian ganglion.

We can confirm his statement from the examination of two cases of zoster within the territory of the trigeminal nerve.

One of our earliest cases (Case 19) was a typical supra-orbital zoster, covering the whole of the first or ophthalmic division of the trigeminal nerve, excepting only that the eruption did not extend to the side of the nose. Death occurred 190 days afterwards, and the Gasserian ganglion showed what appeared to be the remains of an old hæmorrhage with some destruction of nerve-cells in that portion corresponding to the first division.

The root bundles of the affected ganglion showed an appearance that made it probable that a few of them were sclerosed, but there was no acute degeneration in any part of the central nervous system referable to the lesion in the Gasserian ganglion.

In Case 18 death took place thirty days after the outbreak of the eruption, and we found here all the changes, both ganglionic and degenerative, which we have described in cases of zoster affecting the body. In this case an eruption of the zoster type lay over the right lower jaw, limited absolutely to one side of the face. Fig. 18 shows how completely this eruption followed the anatomical distribution of the third or maxillary division of the trigeminal nerve. At death a few lightly scabbed scars were still present over the temporal portion of this trunk.

A comprehension of the position of the ganglionic lesion in this case will be facilitated by considering the Gasserian ganglion as a triangle, from the inner angle of which the greater part of the central root-fibres come off. At the preaxial angle of this triangle the first or ophthalmic division, and at the postaxial angle the third or maxillary division, enters the ganglion. A focus of destruction is seen (plate 9), running almost parallel with the postaxial side of the triangle directly dorsal of the position of the motor root; that is to say, it occupied that portion of the ganglion which stands in direct relation with the maxillary branch.

This focus is roughly oval in transverse section. Its greatest transverse diameter is 1·275 mm.; its greatest vertical diameter 0·765 mm. It appears to be made up of a large central nucleus containing brown material, obviously the broken-down remains of a hæmorrhage and the *débris* of destroyed nerve-cells. This is surrounded by an area abundantly occupied by small round cells and enveloping this area, extending up to the pia on the free surface; and for some distance into the ganglionic substance is a wider zone densely infiltrated with small round cells in which remains only of nerve-cells and nerve-fibres can be seen. The remainder of the ganglion is healthy.

Thus we here find an exact reproduction of the familiar lesion in the posterior root ganglion, and just as the sheath of the spinal ganglion tended to become implicated in the lesion, so over this focus in the Gasserian ganglion the pia shows signs of thickening and infiltration.

Secondary to this lesion there is some degeneration in the root of the fifth nerve. It is principally confined to three small fasciculi lying at the periphery of the transverse section opposite to the motor root. But although the lesion is only thirty days old much of the black material of the broken-down medullary sheaths is already cleared away and sclerotic changes are well advanced; but in the pons and medulla the degenerated fibres still stain by Marchi's method, just as if they were freshly degenerated. Thus here, again, the intramedullary and extramedullary portions of the central projection of a neuron behave exactly as in the spinal cord, and the products of degeneration are removed much more rapidly from the root than from the central nervous system.

In the pons the so-called "descending" or cerebral root is completely free from degeneration, thus confirming the usually accepted view that this is the central portion of the motor root.

The so-called "ascending" or spinal root shows acute degenerative changes. At the point of entry into the pons a few scattered degenerated fibres are seen in all the bundles of the root, but in the outer portion 2-3 fasciculi are gravely affected. These fibres can be followed into the pons, and appear, when close up to the nucleus, to curve abruptly downwards external and ventral to the nucleus (plate 13, fig. 3).

More caudalwards, as soon as the sensory bundle has formed into its pear-shaped area, the degenerated fibres are seen to lie almost entirely in the upper two-thirds of this pear-shaped tract. The lower one-third is practically free from degeneration (plate 13, fig. 6).

No fibres cross to the opposite side. At the level of the seventh nucleus the fibres are cut transversely instead of somewhat obliquely, and they lie almost entirely in the upper two-thirds of the pear-shaped field.

Opposite the great olive the degenerated fibres are less numerous, but are still situated in the upper two-thirds of the field.

Opposite the main decussation of the fillet the root lies between the dorsal half of the substantia gelatinosa Rolandi and the surface. Here the degenerated fibres again lie in the dorsal portion of the field and the ventral portion is practically free from degeneration.

Opposite the 1st cervical root the degeneration is indistinct, but in the most dorsal portion of the substantia gelatinosa an obvious collection of black dots is seen not represented on the opposite side.

Thus we can state for certain that in man the third division of the trigeminal is connected with cells in the Gasserian ganglion which send fibres centralwards to lie in the so-called "ascending" or spinal root. They occupy the dorsal two-thirds of this bundle almost exclusively.

Now the second division of the trigeminal is closely allied to the third division in nature and function in that both supply structures derived from the arches that enclose the first gill slit [*vide* Head (28), p. 476]. It is therefore probable that the remaining undegenerated fibres of the spinal root of the trigeminal belong to the second division.

On the other hand, the first or ophthalmic division stands apart from the other two branches in its curious participation in visceral pain referred from organs of the thorax and abdomen. Thus it is possible that the central projection of the cells which give rise to this division may end around the upper sensory nucleus of the trigeminal nerve. For in the case we have just described the fibres which pass to end around this nucleus do not show any obvious signs of degeneration.

In conclusion, we may state that zoster of the branches of the trigeminal is associated with a similar lesion in the Gasserian ganglion to that found in the posterior root ganglia in cases of zoster of the trunk and limbs.

This lesion causes secondary degeneration in the sensory root of the Gasserian ganglion both in its extra- and intramedullary course.

Chapter 6.—Zoster secondary to implication of the Ganglion in General Disease Processes.

In all the cases that we have so far considered, zoster has arisen as a primary manifestation. Some agent of the nature of which we are ignorant chooses the substance of the posterior root ganglion for its selective activity, producing profound inflammatory changes. These destructive changes in the ganglion produce irritation of its nerve elements, and to this irritation is due the eruption on the skin.

Now it is interesting to find that acute inflammation of a posterior root ganglion, due to its implication in some local inflammatory process, can apparently produce an herpetic eruption indistinguishable from an eruption which arises as manifestation of the acute specific disease.

It is well known that when the secondary deposits of malignant disease attack the spinal column the pain produced becomes intense. This is due to the implication of the central portion of the peripheral nerve-trunks and the nerve-roots in the new growth. It is, however, less a matter of common knowledge that an eruption indistinguishable from that of zoster may also make its appearance. Charcot and Cotard (4), gave a very insufficient report of such a case in 1865, but we can find but one other paper dealing with this subject [Risel (38)].

In Case 14 of our series, a man of 40 suffered from lympho-sarcoma that affected all the large groups of lymphatic glands. Seventeen days before death he developed a severe herpetic eruption over the 4th dorsal area. On *post-mortem* examination the mass of glands in the posterior mediastinum was profoundly affected by new growth and this growth had invaded the spine, passing inwards along the great peripheral nerve trunks into the foramina. The upper seven dorsal foramina on the right side, the side of the eruption, all contained new growths, which surrounded the ganglion and posterior roots. In most cases the posterior roots had suffered and showed degenerative changes, as might have been expected from their delicate structure; but only one of the ganglia showed any inflammatory change. In most cases the tough sheath had resisted invasion by the new growth that could be seen in the periganglionic connective tissue. However, it was noticed at the *post-mortem* examination that the 4th dorsal ganglion of the right side was entirely concealed in the mass of new growth that filled the foramen in which it lay, and the contents of the foramen were therefore removed in their entirety. When the mass so obtained was hardened and cut, it was at once obvious that the ganglion lay in the centre like the stone of a plum. Microscopically the whole ganglion is infiltrated with small round cells, which stain profoundly with methylene blue (Nissl's method). So deeply do these cells take the dye that the whole ganglion may be decolourised and yet they remain overstained. Where these cells are most thickly crowded together remains of ganglion cells can be seen as white or greenish blue discs with an unstained nucleus and quite undifferentiated. These cells take the counter-stain erythrosin readily, and appear as pink undifferentiated bodies in the centre of a mass of small round deep blue inflammatory cells. Where the inflammation is less intense the ganglion cells either stain as uniform blue masses or they show marked chromatolytic changes. The body of such cells presents a granular appearance, Nissl's particles have disappeared and large light patches may be present in the protoplasm when stained by Nissl's methylene blue method, The nucleus is excentric and appears in some cases to have been extruded. In fact, the changes in these cells are those seen in any cell containing portions of the nervous system from which the blood supply has been cut off [Sarbó (39). Mott (34)].

Thus the 4th dorsal ganglion in this case, lying in the centre of a mass of new growth, showed firstly a profound inflammatory change in the interstitial tissue, and secondly changes in the ganglion cells, which ranged from absolute destruction to those chromatolytic changes which we have now learnt to associate with profound disturbance of vital activity.

It is of course possible that this condition was due to the same specific toxic influence that produces primary zoster, and that the condition of the 4th dorsal ganglion, surrounded as it was by new growth, laid it particularly open to attack by the specific disease process. But it seems far more probable that in this case the zoster was directly produced by the secondary inflammation produced in the ganglion by the new growth. It is also certain that so considerable a mass of malignant growth in the foramen must have interfered materially with the blood supply.

In the next case of our series (Case 14) we believe the zoster that made its appearance shortly before death to have been due to direct interference with the ganglion in consequence of injury to the spine.

A man of 36 was struck on the back by a descending lift, and immediately lost motion and sensation below the umbilicus. The analgesia was sharply limited by the upper borders of the 10th dorsal area, but above this area lay a band of intense hyperalgesia, corresponding to the 7th, 8th and 9th dorsal areas on both sides. Six days before his death a small patch of herpetic eruption appeared over the tip of the ninth and tenth costal cartilages.

On *post-mortem* examination the transverse processes of the 11th dorsal vertebra were found to have been fractured, and the 11th and 12th dorsal vertebræ had gone bodily backwards. The 10th, 11th and 12th dorsal ganglia on both sides were surrounded by a mass of inflammatory tissue, and the posterior roots were destroyed partly by actual trauma, partly by inflammation. These changes exactly corresponded with the analgesia discovered during life.

But in addition to these direct traumatic changes, the cells of the 8th, 9th, 10th, 11th and 12th dorsal ganglia on both sides showed profound chromatolytic changes. Thus the disturbance of the ganglion cells was not limited to those ganglia which were implicated directly in the injury (10th, 11th, 12th dorsal), but also extended to the 8th and 9th dorsal, which were not surrounded by inflammatory tissue. Moreover, the 7th, 8th and 9th dorsal posterior roots on both sides showed a curious alteration, in that their medullary sheaths were swollen, their vessels were engorged, and leucocytes were freely extravasated with the connective tissue between the nerve-fibres. We believe that these changes in the ganglia are probably due to interference with their vascular supply, and account for the hyperæsthesia that was present over the 7th, 8th and 9th dorsal segments.

Lastly, the 9th dorsal ganglion stood alone in showing a small focus of inflammatory small round cells situated close to the point where the central vessel of the ganglion gives off its lateral branches. This focus is an extremely small one and can only be taken to explain the small patch of zoster that appeared over the 9th space shortly before death in the light of the other cases we have reported.

This case seems to us to explain the appearance of herpes zoster in cases of caries of the spine. One of us has observed three cases in which an outbreak of zoster corresponded with renewed activity of the tubercular process in the spine. In two of these cases the outbreak of zoster followed the leaving off of a poroplastic support that had been worn for years. Shortly after the support was laid aside pains in the chest and epigastrium appeared, followed, by an attack of zoster that corresponded in the one case to the 5th dorsal in the other to the 7th dorsal area.

Thus, in conclusion, it would appear that zoster in all respects resembling that arising spontaneously may be produced by implication of a posterior root ganglion in inflammatory processes secondary to malignant disease, tubercle or injury.

Chapter 7.—*Zoster arising in the course of Disease of the Nervous System.*

In tabes dorsalis outbreaks of zoster form a classical symptom, but this phenomenon is rarer than the text-books would lead us to suppose. One of us, who has seen large numbers of cases of zoster and of tabes during the last eight years, has only met with the conjunction three times. In one case the zoster lay over the area of the third cervical, and was indistinguishable from a severe attack in an otherwise healthy patient. The other two eruptions differed from the common form in that they were scanty, incomplete and tended to come out over a longer interval, which in one of the cases extended to four weeks.

Some light is thrown on this association by Case 17. This man was admitted to Rainhill Asylum for dementia paralytica, but his knee-jerks were absent, and although he could walk he had ataxy of the arms. Thus he was not only a tabetic general paralytic, but was at the same time ataxic. Now it is not uncommon for cases of dementia paralytica to have no knee-jerks and, after death, on microscopical examination of the spinal cord, to show the characteristic lesion of tabes. But it is in our experience less common for such cases to be markedly ataxic during life.

Thus, although this case was one of dementia paralytica, the signs of tabes were so marked that it throws some light on the condition of the nerve-roots in this disease which favours the development of attacks of zoster.

The eruption fell over the 8th dorsal area, and, as in two of the other cases occurring in tabetics, was not profuse.

The 6th, 7th, 8th, 9th and 10th dorsal roots were examined on both sides, and of these several show the following changes:—The sheath of pia mater reflected on to the posterior nerve roots from the spinal cord presents a general inflammatory thickening, and is densely infiltrated with small round cells. In many instances the inflammatory exudation has penetrated the perineurium of individual nerve bundles and given rise to a change in them.

This change is most advanced in the 8th dorsal root of the left side, and here it is not confined to the posterior root, but had spread to the sheath of the ganglion. Running round about one-sixth part of the circumference of the ganglionic sheath, partly upon it and partly within its lamellæ, is a dense collection of small round cells about as deep as the sheath itself. Within the ganglion itself are a few foci of small round-celled infiltration.

Slight as these changes are in the ganglion compared with those in many of the cases we have described above, it is certain that they coincide with a difference between the condition of the 8th dorsal ganglion of the left side and its fellows, for the entry of the 8th dorsal root into the cord on the left side is marked by a field of acute degeneration, which passes up to be lost at the level of the 8th cervical in the usual manner.

This thickening of the pia arachnoid over the dorsal surface of the cord and around the roots is a common condition in cases of tabes; so much so that Obersteiner looks upon it as the essential lesion. Now it would appear that our case shows little more than an extension of this process to the sheath of the ganglion, and just as the small round-cell infiltration had penetrated between the fibres of the posterior root, so the similar change in the sheath of the ganglion had penetrated the substance of this structure. But, on the other hand, it is possible that the changes in the root and in the vessels which are present in tabes had rendered the ganglion more vulnerable to an attack of primary zoster. We are, however, more inclined to the view that the zoster in this case was directly secondary to the disease process of tabes than to the latter hypothesis.

The next case in which zoster appeared in the course of gross organic disease of the spinal cord and roots (Case 16) presents greater difficulties. An eruption, differing in no way from that of spontaneous zoster, appeared, over the 3rd cervical area in a patient suffering from multiple sclerosis secondary to endarteritis obliterans of the small vessels of the nervous system. At the level of the 7th and 8th dorsal roots this vascular change had gone on to complete obliteration of the vessels supplying the anterior half of the spinal cord. This had caused that portion of the cord to be converted into a necrosed mass enclosed in a thickened membrane. Elsewhere in the cord the change was not so advanced, and patches of irregular sclerosis were seen surrounded on their free borders by acutely degenerated fibres (Marchi).

The posterior roots in this case present a singularly interesting condition. When treated by Marchi's method they do not stain well, but become pale and ash gray in colour. Their outlines are indistinct and many of the fibres are slightly swollen. Although none of them show any clearly-marked acute degeneration, leucocytes containing fat and many irregular fat globules are seen lying between the fibres.

The 3rd cervical ganglion on the left side shows many foci of small round inflammatory cells, with destruction of ganglion cells closely resembling the changes seen in ordinary cases of spontaneous zoster, except that we are able to find no hæmorrhages.

We are inclined to think that the zoster in this case was not the direct outcome of the disease of the nervous system from which this patient suffered, but that the endarteritis obliterans and the changes it produced in the whole nervous system predisposed the ganglion to attack by the same unknown agent that produces zoster in otherwise healthy persons.

Amongst the first thirteen cases of our series which we have classed as spontaneous zoster occur three cases in which the outbreak appeared in patients suffering from dementia paralytica (Cases 6, 9 and 10). It might be thought that such cases should have been associated more rightly with those in the present Chapter, but in none of these cases were any lesions of the spinal cord present other than degeneration in the lateral columns, and the roots were unaffected with the exception of that root passing out of the affected ganglion. Moreover, the nature of the ganglionic lesion differed in no way from that found in the other cases of the spontaneous series.

General paralysis or dementia paralytica undoubtedly disposes to zoster. But this is probably due, not to any direct implication of the ganglia of the posterior roots in the disease process of general paralysis, but to general susceptibility induced by the circulation in the blood of these patients of toxins produced by the breaking down of the higher centres [Mott and Halliburton (35)], by the vascular changes so commonly present in, and the general debility produced by, this disease. Such patients are in the same way unduly susceptible to attacks of acute lobar pneumonia and of dysentery.

Chapter 8.—*Changes in the Skin and Glands.*

§ 1. *Changes in the skin.*—Sections through an unruptured vesicle of herpes zoster show a cavity, the floor of which is formed of naked papillæ. These papillæ are in a condition of profound inflammation and are infiltrated with masses of small round cells which stain deeply. This infiltration with small round cells extends down to the terminations of the sweat glands and hair follicles and here and there small collections of small round cells are seen in the deeper layers of the skin even apart from the hair follicles and sweat glands.

The vesicle is split into incomplete cavities by septa extending from the roof to the floor. These septa are evidently the remains of incompletely-raised epithelial layers that retain their attachment to the roof and to the floor of the vesicle. The cavity of the vesicle is filled with fluid that coagulates under the influence of the hardening agent into a somewhat granular hyaline mass. Within this mass lie small round deeply-staining cells and broken-down epithelial cells of all sizes and shapes which have lost their prickles.

We have traced nerve twigs up to the portion of skin excised for examinations and found that they showed marked signs of degeneration by Marchi's method, but we have not succeeded in demonstrating degenerated fibres in the actual portion of skin examined.

In 1889, Pfeiffer (21), taking up a position opposed to the nervous origin of herpes zoster, laid stress on certain cells he found in the vesicles. They had a diameter of 30 μ and also occurred in the vesicles of varicella and vaccinia. He nowhere definitely stated they were parasites, but his mind evidently leant in that direction, for he gives a considerable description of diseases caused by protozoa. Hartzell (20) rightly recognised that they were epithelial cells that had undergone degenerative changes. We have seen them in one of the cases we examined, but not in Case 2.

Dr. Hunter, assistant bacteriologist to the London Hospital, has kindly examined the unbroken vesicles in five cases. In most of these cases we took serum from two or more vesicles. In every case the contents of the vesicles were sterile.

Moreover, microscopic examination of the fluid and careful staining of the sections of skin failed to reveal any sign of micro-organisms. Dr. Bulloch kindly stained some specimens of skin in Case 2 and confirmed this result to which we had arrived in other cases.

§ 2. *Changes in the glands.*— The lymphatic glands enlarge and frequently become tender very early in the disease. It is interesting to note that apparently all the areas of the thorax above the 7th dorsal drain into the axilla, whilst all below this area drain into the groin. The 7th dorsal itself and sometimes the 8th dorsal may cause enlargement of either the axillary or inguinal lymphatic glands, or even of both sets.

In Case 2 the enlarged axillary glands were incised two hours after death under rigid aseptic precautions by Dr.

Bulloch, the Bacteriologist to the London Hospital. He could obtain no evidence of bacterial invasion, and sections of the glands revealed no micro-organisms.

But these sections show that the glands were in a profound condition of inflammation. Masses of small round cells can be seen not only in the substance of the gland but also in the trabeculæ.

Thus we are brought face to face with the curious fact that a collection of intensely inflamed vesicles containing a sterile fluid can be associated with enlargement of the lymphatic glands. Moreover, these glands have all the appearance of being inflamed, and yet show no sign of bacterial invasion.

Chapter 9.

§ 1. *Herpes zoster, an acute specific disease of the nervous system.*—A typical attack of zoster arises without any obvious peripheral or central cause, and must be considered an acute specific disease of the nervous system, for it starts with a prodromal period of varying length, during which the temperature is raised. During this period the patient feels ill and has more or less pain; but it is then impossible to make a diagnosis. If the patient is a child, he may be supposed to be sickening for one of the ordinary acute specific diseases. Suddenly, however, after a variable period, the rash comes out and the disease declares itself. The febrile period lasts from three to five days and this may be considered the duration of the acute disease. The rash may appear a few hours after the onset of the disease or may tarry till the fall of temperature. Thus, if the rash be taken to represent the physical signs, an attack of zoster may be compared in these characteristics with an attack of acute lobar pneumonia. For as is well known the signs in the lungs in this disease may be present very shortly after the initial rigor, or may not make their appearance until the crisis is reached. The rash in herpes zoster most commonly makes its appearance on the third or fourth day of the disease, just as the physical signs of acute lobar pneumonia usually become evident on the third or fourth day after the initial rigor.

If zoster be an acute specific disease, second attacks should be uncommon, and we find as a fact that second attacks are less common than second attacks of measles. We have met with only four such instances in over four hundred cases. Again, the disease should tend to occur more at certain periods than at others or even appear in actual epidemics. This is now recognised to be the case. The records kept by one of us at the London Hospital tend to bear out this statement; for, although sporadic cases occur throughout the year, at certain seasons there is a large increase in the number of cases. Thus, in 1896, 1897 and 1898, there was an epidemic in the middle of March. In 1897 and 1898 there was an outbreak from the middle to the end of May. In 1897 a large number of cases appeared during the long drought that lasted from the end of July until the beginning of November; and during this period of four months fifty-eight cases were seen, or one half the cases of that year. In 1898 several cases appeared together in June, and there was a marked outbreak from the middle of July to the end of August, during which period twenty-two cases were seen in less than six weeks. In the same year another outbreak occurred in the middle of October. Thus there can be little doubt that the occurrence of epidemics of herpes zoster is associated with some atmospheric influence or conjunction of which we are as yet ignorant.

But if herpes zoster is an acute specific disease of the nervous system we find an exactly analogous disease in acute anterior poliomyelitis. This disease begins with malaise and fever. The temperature may remain raised for from three days to a week, and at a variable time during this febrile period, or it may not be until the fever has subsided, paralysis is noticed.

On comparing the pathological condition discovered on microscopical examination in the two diseases their likeness becomes still closer. The following summary of the conditions found in those cases that have died at varying periods in the first few months, given by Allan Starr (45), exactly corresponds to what can be seen in two cases of this disease we have had the opportunity of examining.[1]

"On microscopical examination there is found a marked hyperæmia of the tissue; all the blood-vessels are engorged and surrounded by exudation alike of serum, of leucocytes, and of small cells. The serum fills the lymph spaces about the vessels and about the nerve-cells. The leucocytes infiltrate the tissues about the cells and cluster around them. There is a great increase of small cells and nuclei in the neuroglia. . . This infiltration of the tissue with leucocytes may be so intense as to obscure all other elements. Ruptured capillaries and small hæmorrhages are seen here and there. It is thus evident that the supporting substance (neuroglia) of the grey matter and the blood-vessels are involved in the inflammatory process.

"The changes in the ganglion cells of the cord are equally characteristic. These cells show great varieties of degenerative changes depending partly upon the severity of the case and partly upon the length of time the process has been going on in any one cell. The earliest change in the cell is the cloudy appearance of its protoplasm, and increased granular appearance obscuring the nucleus and leading to its deeper staining by reagents. In the next stage the cell absorbs stains no longer; the nucleus is faint and the cell has lost its sharp outline and some of its prolongations. Later still the cell appears changed into a swollen, shapeless or spherical ball of matter, and its protoplasm is altered into a homogeneous unstained mass with vacuoles, or has become distinctly granular, in which case it stains deeply. . . The last stage is one of shrinkage, the cell body being changed into a small, deeply-stained mass hardly larger than its original nucleus. . . . . If the case be examined some weeks or months after the onset the vascular changes are no longer evident; the serous exudation has been absorbed, there are no longer leucocytes and cells within the interstitial tissues. . . In some parts the anterior horn may be changed even into true sclerotic tissue."

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[1] We owe the opportunity of studying one of these cases to the kindness of Dr. Mott, who has incorporated it in his Croonian Lectures (34). Sections of the other case were kindly given us by Dr. Bulloch.

If for anterior horn we read posterior root ganglion, and for motor cell posterior ganglion cell, this statement would be an exact description of the changes we have described in Chapter I.

Moreover, the posterior root ganglion is the exact equivalent of the anterior horn. For whereas on the motor side the cells of the neurons of the lowest level lie in the anterior horn, on the afferent side, they happen to lie collected together outside the spinal cord in the posterior root ganglion. Thus zoster might justly be spoken of as acute posterior poliomyelitis.

§ 2. *The nature of the changes that produce herpes zoster.*—The changes which we have described above in the posterior root ganglion, closely resembling as they do those found in the grey matter of the anterior horn in acute anterior poliomyelitis, are typical of a pathological process in the nervous system that has of late years been too much neglected. It is usually dismissed by the statement that it is "of vascular origin." Now if by "vascular" is meant that the disease is directly secondary to occlusion or interference with a vessel, we deny its correctness; if, on the other hand, it is simply meant that the vessels play an important part in the general inflammatory process, it is a platitude.

Many observers have occluded the vessels of the spinal cord for varying periods, and examined the changes so produced in the cells. Such occlusion of the arteries produces marked chromatolytic changes in the cells of the spinal cord, but is not followed by inflammatory changes or hæmorrhages. Leonard Hill ligatured the cerebral arteries in monkeys, and the brains of these animals were examined by Mott (34) at varying periods after the operation. Here, again, extreme chromatolysis of the cortical cells was found, but no inflammatory changes and no hæmorrhages.

Now the universal characteristic of the changes we have described in the affected ganglion is the presence of inflammation in every degree, from scattered collections of small round cells to profound hæmorrhages in the centre of inflammatory foci. On the other hand, our cases of spontaneous zoster did not show marked chromatolytic changes of the type seen when either the vessels of the spinal cord or of the brain were experimentally occluded. A certain number of ganglion cells seem to be killed outright, and others to be so injured that they quickly die. The remainder, however they may have been changed at the onset of the disease, rapidly recover. Very few, if any, of the ganglion cells appear to be undergoing that steady process of disintegration which we have learnt to associate with the appearances known as chromatolysis.

It is therefore peculiarly interesting to notice that in the two cases of secondary zoster, where we have every reason to suppose that the blood supply of the ganglion was profoundly affected, chromatolytic changes were well marked. In one of these (Case 14), the ganglion was completely surrounded by malignant growth, and in the other (Case 15), the spine had been fractured.

Moreover, secondary degeneration makes its appearance within eleven days of the appearance of the eruption over the whole central projection of the fibres, large and small, in connection with the cells of the posterior root ganglion. This looks far more as if the process were one of acute destruction of ganglion cells than of damage by a poison leading to degeneration and death of the nerve-cell.

Thus it would appear that the changes in the posterior root ganglion consist of an acute interstitial inflammation accompanied by necrosis of the ganglion cells.

Of the nature of the agent which is responsible for this process we are completely ignorant. Microscopically, we have not been able to find any signs of bacterial infection, but have not attempted to make cultivations for fear of spoiling our material for other purposes.

But this agent, whatever it may be, seems to have a specific attraction for the posterior root ganglion exactly as the equally unknown cause of acute anterior poliomyelitis attacks the substance of the anterior horns. Moreover, it is particularly liable to attack the dorsal part of the ganglion, *i.e.*, the portion opposite to the anterior root.

Each posterior root ganglion is supplied by a branch of the arteries in front of the spine (intercostal, &c.). This twig passes in with the peripheral nerve, and courses through the ganglion to meet the branch of either the anterior or posterior spinal arteries. In the ganglion this artery gives off branches towards the periphery, and it is around the terminations of these small branches that hæmorrhages are most often found. Owing to the anastomosis between the arteries of the spinal cord and the branches on the anterior surface of the spine, the ganglion can be injected with colouring material from both directions. If the hæmorrhage is severe it may transgress the territory of the ganglion and occupy the centre of the peripheral nerve (Cases 2 and 4).

It is probable that two ganglia are occasionally affected together. From clinical observation this seems particularly liable to occur with the 2nd, 3rd, and 4th cervical. Unfortunately, no such case is included in our series of *post-mortem* examinations. One case has come under our notice where a true zoster was present at the level of the 8th dorsal on one side and of the 10th dorsal on the other at the same time. Such cases are, however, excessively rare; a similar one has been reported by Kaposi.

Thus the unknown agent responsible for the inflammation in the ganglion not only shows a specific attraction for the posterior root ganglia but commonly attacks one ganglion only. This selection of one group of cells is also partly characteristic of the poison that causes acute anterior poliomyelitis, but as the gray matter of the anterior horns forms a continuous column the inflammatory process has more opportunity of spreading upwards and downwards than in the case of the segmented groups of posterior nerve-cells collected as they are into separate and distinct ganglia.

But we have also to deal with the curious fact that some ganglia seem to be more prone to attack than others, as is shown by the following table compiled from records of 392 cases. No cases are included in which an area was seen in combination with one above or below it.

2nd Cervical	1	3rd Dorsal	34	12th Dorsal	18
3rd ,,	15	4th ,,	38	1st Lumbar	27
4th ,,	21	5th ,,	38	2nd ,,	22
5th ,,	2	6th ,,	20	3rd ,,	5
6th ,,	3	7th ,,	19	4th ,,	1
7th ,,	5	8th ,,	36	5th ,,	2
8th ,,	0	9th ,,	19	1st Sacral	0
1st Dorsal	5	10th ,,	26	2nd ,,	1
2nd ,,	9	11th ,,	22	3rd ,,	5

It will be seen from this table that the ganglia most commonly affected are those which receive afferent impulses from the viscera through the white ramus of the sympathetic (*cf.* Head 30).

Now if any posterior root ganglion is carefully examined it will be found to contain two main groups of cells, large coarsely granular nerve-cells and smaller more pear-shaped cells that stain with methylene blue in a more uniform manner.[1] But the proportion of these two types of cell in any one ganglion varies according to its position. Thus the 6th, 7th, and 8th cervical contain a much larger proportion of large cells than of small ones, whilst from the 3rd dorsal to the 1st lumbar the small cells preponderate. In the 2nd, 3rd, and 4th cervical there is a great preponderance of small cells over large.

Thus the ganglia which receive fibres from the limbs, especially those which receive theirs from the hand (cervical 8) and foot (sacral 1) show a preponderance of cells of the large coarsely granular type. Now, these areas are exactly those which give rise to the long fibres of the posterior columns. For as many observers have pointed out from experiments on animals, and as our observations confirm for man (*vide* p. 374) the postero-internal column in the cervical region is mainly formed by fibres from the leg area, the postero-external by fibres from the arm.

Thus, it would appear that the toxic agent that produces herpes zoster not only has an affinity for the posterior root ganglia, but more particularly for those which contain a preponderance of the smaller type of ganglion cells that give rise to the shorter fibres of the posterior columns.

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[1] There is also probably a difference in the processes of these two types of cell, but this will form the subject of a further communication.

But when once a ganglion is attacked all the cells within the area of inflammation suffer, whether they be of the large or small-celled type.

Now these small cells amongst other functions probably subserve that of pain, for Münzer (36) has shown that the long tracts of the posterior columns do not conduct pain impressions to the cerebrum. Hence the intense pain which accompanies an attack of zoster.

But if the case be seen before the rash appears it is sometimes possible to map out the area subsequently occupied by the eruption by means of the hyperalgesia that is present. This hyperalgesia, which closely resembles that so frequently seen as the concomitant of visceral referred pain, is followed by erythema. Then, on the erythematous surface, vesicles appear.

Thus we are inclined to think that the trophic disturbance of the skin is an extreme form of activity of the same cells, disturbance of which by afferent impulses along the white ramus produces the hyperalgesia that accompanies visceral referred pain.

We do not imagine that the eruption of herpes zoster is produced by disturbance of special trophic nerves, but by intense irritation of cells in the ganglion which normally subserve the function of pain, and more particularly that form of pain produced by afferent visceral impulses.

PART II.—THE BEARING OF THE DISTRIBUTION OF THE ERUPTION IN HERPES ZOSTER ON SENSORY LOCALISATION.

Introduction.

Before this research began one of us had collected a large number of cases of herpes zoster and had constructed a diagram to show the relation that the areas occupied by the eruption bore to one another. A series of segments was thus mapped out upon the surface of the body, and to each segment was given a hypothetical number which was supposed to represent its numerical localisation in the central nervous system. This numerical localisation met with universal disbelief, alike from anatomists and clinicians, and it was therefore felt that if a *post-mortem* examination could be obtained on a case of herpes zoster in which the distribution of the eruption had been carefully drawn or photographed, the question might be settled one way or the other.

But herpes zoster is not a fatal disease, and we felt that the only method by which we could obtain the material we desired was by the study of patients in asylums or infirmaries, a considerable proportion of whom remain in the institution until their death. By this means we have obtained fourteen out of the twenty-one cases we have examined; of the remaining seven cases, we owe three to the kindness of the physicians of Guy's Hospital and four were collected by one of us at the London Hospital. At the same time one of us has collected drawings or photographs of 450 cases that have come under his personal observation.

This material enables us now to deal with the question of numerical localisation in a complete manner. But we wish it to be clearly understood that the segmental areas to which we refer in this paper are those marked out on the skin of the body by the eruption of herpes zoster, and when we speak of an area as, *e.g.*, "the 4th dorsal," we mean that that area corresponds with disturbance of the 4th dorsal ganglion. The question of the identity in position and constitution of these areas with the areas of hyperalgesia that accompany the referred pain of visceral disease, and the relation of these areas to the territory supplied by each posterior spinal root, will be dealt with subsequently by one of us in a separate paper.

On plate 17 we have attempted to combine the typical distribution of each area on a single diagram. Such an attempt is in itself fallacious, for no such combined figure can be absolutely accurate; for on the trunk each area is a band coiled round one half of a rough cylinder, and must therefore vary in each case according to the shape of the trunk. Thus one of these areas extended around the abdomen of a baby will have a completely different appearance from the same area around the waist of a woman who wears stays. An eruption produced by a lesion of the 6th dorsal ganglion will differ considerably when extended on the narrow sloping chest of the phthisical or on the barrel-shaped, high shouldered thorax of the emphysematous. Bony points are thus almost useless: skin points only are trustworthy, and of these we unfortunately possess only the nipple and the umbilicus.

We are also confronted with another difficulty which must always make such a combined diagram incomplete; for the supply of the afferent ganglionic fibres is subject to variation, and any one portion of skin may be supplied in the one patient by the fibres that enter one ganglion, in another by those that enter the ganglion above or below. We hope, however, to be able to show the extent to which this variation may occur and the laws by which it is governed.

Lastly, we shall deal with the question of interdigitation and overlap in as far as it affects the areas mapped out on the body by the eruption of herpes zoster.

§ 1. *The numerical localisation of the areas marked out by the eruption of herpes zoster.*—When the original diagram of the areas on the surface of the body was published by one of us (27), Thane (46) summed up the criticism of the anatomists in the following passage:—"It may be pointed out that the areas as designated do not always agree with the distribution of the corresponding nerves as determined anatomically. Thus the area marked D 3 on the inner side of the arm corresponds rather to the brachial distribution of the 2nd dorsal nerve through its intercosto-humeral branch and the communication with the nerve of Wrisberg, while the third dorsal nerve does not usually contribute largely to the supply of the arm. Similarly the areas marked D 11, D 12, and L 1, would seem on anatomical grounds to correspond more nearly to the 12th dorsal and 1st and 2nd lumbar nerves."

Thorburn (48), is equally definite: ". . . If we trace Head's areas downwards we find other evidences of a tendency to describe them as being a segment or part of a segment too high. . . . If, however, we turn to the lower part of the diagram there appears to be a tendency in an opposite direction, that is, the areas are depicted too low. Thus it will be seen that his 1st lumbar region corresponds more closely to that which Starr and others besides myself assign to the 2nd lumbar, and anatomical dissection shows that the 1st lumbar nerve is mainly distributed above the line of Poupart's ligament where Head has the 12th dorsal . . . and finally, the umbilicus probably lies, not as Head places it at the junction of the 9th and 10th dorsal fields, but certainly no higher than the lowest part of the 10th."[1]

The combined diagram we give differs somewhat from that on which these criticisms were written, but the differences lie in the form of the areas and not in their general position. A greatly increased number of cases has enabled us to bring the form of the various bands more nearly to that which we consider normal. But we still maintain that the 3rd dorsal usually supplies part of the inner side of the arm, that the 5th dorsal sends fibres to the lower part of the breast, that the umbilicus lies between the 9th and 10th dorsal areas, and that the 12th dorsal supplies the skin partly above and partly below Poupart's ligament.

The following table of the segments from the 3rd cervical to the 1st lumbar shows those we have examined :—

Cervical 3.—Examined twice. Case 6, fig. 6, and Case 17, fig. 17.
Cervical 4.—Case 10, fig. 10.
Cervical 5.
Cervical 6.
Cervical 7.
Cervical 8.
Dorsal 1.
Dorsal 2.—Case 7, fig. 7.
Dorsal 3.
Dorsal 4.—Examined twice. Case 11, fig. 11, and Case 14, fig. 14.
Dorsal 5.
Dorsal 6.—Examined twice. Case 3, fig. 3, and Case 13, fig. 13.
Dorsal 7.—Examined twice. Case 2, fig. 2, and Case 9, fig. 9.
Dorsal 8.—Case 16, fig. 16.

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[1] The interesting monograph by Wichmann, "Die Rückenmarksnerven und ihre Segmentbezüge," did not reach us until our paper was already in print. As far as the trunk is concerned, his figure of the sensory segments more closely resembles that of Head (30) than any other scheme. However, he places the umbilicus in the centre of the 10th dorsal field.

Dorsal 9.
Dorsal 10.
Dorsal 11.—Case 5, fig. 5.
Dorsal 12.—Examined three times. Case 4, fig. 4; Case 8, fig. 8; and Case 12, fig. 12.
Lumbar 1.—Case 1, fig. 1.

Thus out of nineteen consecutive areas we have examined ten, and of these ten we have examined five more than once.

Amongst these cases we are fortunate in having several that include the disputed points. Thus Case 11 and Case 14 show how the 4th dorsal lies above the nipple, supplying, in a woman with large breasts, the upper half of the mammæ and sending a branch to innervate the upper half of the areola.

The 11th dorsal, and not the 12th, supplies the groin just above Poupart's ligament (Case 5), and thus it is certain that the umbilicus lies between the 9th and 10th dorsal areas.

Again, we are fortunate in having examined in three cases the 12th dorsal area, upon which universal doubt has been thrown (Case 4, Case 8, Case 12). The extent of the eruption varied in each of these cases, and the conditions of this variation will be considered in the next section. But in all these cases the eruption lay below the crest of the ilium, and extended on to the outer side of the thigh below Poupart's ligament. Moreover, as additional proof, we have examined one case of the first lumbar area, which, though the rash had not developed in front, it was sufficiently well marked, posteriorly and laterally, to confirm the numerical localisation.

Thus if ten out of nineteen consecutive areas have been found by *post-mortem* examination to be correctly numbered, it is unlikely that there is any serious error in the numbering of the remainder.

§ 2. *Variation in form without variation in nerve supply.*—The primitive form of these segmental areas is a band passing around the body from mid-dorsum to mid-venter. The 6th dorsal still retains this primitive character in an almost unaltered form. It starts from the mid-dorsum opposite the 7th and 8th dorsal spines, and passes forward beneath the angle of the scapula. It dips a little in the axilla and swings forward beneath the lower border of the mamma to end in front over the fifth interspace. In its course it passes over the eighth, seventh and sixth intercostal spaces.

If the eruption over this band-like area is examined carefully it is seen to be made up of three main outbursts. The most posterior of these extends from the middle line of the back to about the line of the angle of the scapula, and obviously represents the supply of the posterior primary division. A second outburst takes place in the axilla, and from this point the eruption streams backwards and forwards, representing the lateral cutaneous branch of the anterior primary division. Lastly, over the fifth space in front of the nipple line is a third small outburst corresponding to the terminal twigs of the anterior primary division.

Thus in its complete and primitive form each of these segmental areas consists of a dorsal, a lateral and an anterior division. It is by the changes in the relative proportions of these three constituents that the areas in different regions arrive at their peculiar shape. Passing upwards from the 6th dorsal, we find a tendency for the lateral outburst to be pulled upwards towards the apex of the axilla. This tendency to lateral extension is still more marked in the 3rd and 2nd dorasl, where the lateral flap extends on to the ulnar surface of the arm and reaches its culmination in the detached lateral flap of the 1st dorsal, with its minute anterior and posterior flaps.

Below the 6th dorsal the posterior flap tends to extend downwards on the back, so that its ventral apex may lie below the dorsal apex of the lateral portion of this area. At the same time the lateral and anterior branches of the anterior primary division tend to form a rough triangle on the abdomen. The lower border of every area below the 6th is pulled somewhat downwards towards Poupart's ligament, but rises again towards the middle line of the abdomen. Thus the 9th dorsal area does not touch the middle line of the abdomen at any point below the umbilicus, but its lower border frequently lies considerably below the horizontal level of the umbilicus.

With the 1st lumbar on the front of the thigh and on the buttock, this tendency for the lower border to become dragged downwards becomes well-marked, reaching its culmination in the extraordinary shape of the 3rd lumbar. Below the knee the 4th and 5th lumbar and 1st sacral have entirely lost their anterior and posterior attachments, and consist of the remains of the lateral flap only.

Now it is at once obvious that such a condition offers many opportunities for variation apart from any change in the actual nerve supply. For such an area as the 10th dorsal spread round the abdomen of an infant is a broad almost horizontal band; but on the waist of a woman, especially if she belong to the long-chested type, this area comes to resemble two triangles, in each of which the widest angle is directed towards the leg. The trunk of an infant so much more nearly resembles a cylinder that all the areas, from the 3rd dorsal to the 1st lumbar, tend to become horizontal bands, whereas in the adult they more nearly resemble a couple of obtuse-angled triangles.

Then, again, the trunk of an infant forms a proportionately much larger part of the whole body than in an adult. Thus the areas on the front of the thigh of a young child appear to be smaller and more band-like than those of an adult.

The distribution of these segmental areas on the breast requires special consideration. We will begin with the chest of a young male where the nipple is situated over the lower border of the 4th rib. In such a case the anterior limb of the 3rd dorsal will send a minute downward tag that almost reaches the inner side of the base of the nipple. The anterior axillary branch of the 4th dorsal sends a tag that runs upwards and forwards to end on the outer side of the nipple, whilst the small anterior flap supplies the upper and anterior portion of this structure (fig. 14, Case 14). Thus at least one-quarter of the nipple lies below the lower border of the 4th dorsal area. The 5th dorsal sends an upward projection from its upper border to envelop this portion of the nipple.

This description also applies to the undeveloped breast of a young girl; but as soon as the breast of a woman increases in size, the appearance of these three areas alters profoundly, although on analysis their relations to one another are seen to remain unaltered. The downward tag from the 3rd dorsal becomes of much greater importance, covering a considerable portion of the upper surface of the breast. The forward branch of the lateral flap and the termination of the anterior primary division now become a very prominent feature of the 4th dorsal area, and supply the whole outer and the whole inner quadrant of the mammæ (fig. 11, Case 11.). The 5th dorsal supplies the whole under surface of the mammæ, except that when it is considerably enlarged as in a suckling woman, the upper border of the 6th dorsal laps onto that part which lies over the fifth space and sixth rib.

Into this category we are inclined to place the different appearances presented by the eruption in the three cases where the 12th dorsal ganglion was found to be affected. We regard fig. 8 (Case 8) as the most usual appearance of this area, for it corresponds with the majority of the cases where this area was represented amongst the 450 of our collection. In fig. 12 (Case 12) the downward projection on to the thigh is much less marked, whilst in fig. 4 (Case 4) two long streamers occupy much more of the outer side of the front of the thigh. Yet in all these cases the superior border occupied the same position and the point reached by all three cases in the mid-ventral line was identical.

Thus in conclusion we wish to point out that these areas may differ markedly in different individuals owing to variations in the surface of which the skin is stretched without any necessary alterations in nerve-supply.

§ 3. *Variation in nerve-supply.*—In order to investigate to what extent these areas were liable to true variation, it became necessary to select one of them and to examine as many cases as possible where the eruption lay over that area.

The area selected for this purpose must be easily localised, have well marked anterior, posterior and lateral flaps, and occur with sufficient frequency in a complete form. These conditions are best fulfilled by the 3rd dorsal.

The form assumed by this area, which we consider to be normal, is characterised as follows: The upper border of the posterior flap starts at the 3rd dorsal spine, slopes slightly downwards and then rises to cover the spine of the scapula. From this point it slopes downwards towards the arm to be continued into the posterior border of the lateral flap. The lower border starts behind, about an inch below the upper border, but then slopes rapidly downwards over the scapula, rising again with the external border of that bone to enclose a triangular patch somewhat resembling in shape the lower part of the scapula itself.

The lateral flap covers the upper half or two-thirds of the post-axial border of the arm. Thus, when the arm is raised to a vertical position, with the ulnar border of the forearm and the little finger facing the observer, the lateral flap should appear in its entirety extending one-half or two-thirds of the distance towards the elbow.

The upper border of the anterior flap touches the lower border of the second rib, and the lower border dips on to the region of the mamma to reach a point just above the areola of the nipple. From this point it rises to end over the third rib cartilage.

Out of twenty complete cases in which the eruption lay over the 3rd dorsal, twelve followed exactly this course.

Now if this area were prefixed, *i.e.*, moved up somewhat nearer the head end of the nervous system, we should expect it to show a closer resemblance to the 2nd dorsal than when it assumes what we have called the normal form. That is to say, the upper border of the posterior flap would lie along or above the spine of the scapula and the lower border leave a considerable part of the subspinous portion of the scapula uncovered. The lateral flap would extend further down the axillary border of the arm and nearly reach the elbow. The upper border of the anterior flap would run along the upper border of the 2nd rib, and the lower border would end some considerable distance above the nipple.

This was exactly the area occupied by the eruption in one case out of the twenty cases.

If, on the other hand, this area were post-fixed, *i.e.*, pushed nearer the tail end of the nervous system, it would more closely resemble the 4th dorsal than normal. The upper border of the posterior patch would scarcely touch the spine of the scapula and the lower border would come closer to the angle of this bone, covering a larger portion of the subspinous area. The lateral flap would be shortened so as only to occupy a few inches of the axillary border of the arm. The upper border of the anterior patch would lie over the 3rd rib and the lower border would send a downward tag to envelop the nipple from above.

This condition occurred in seven out of the twenty cases.

Thus out of twenty cases where a well developed eruption occupied the area of the 3rd dorsal, twelve were what we have called normal, one was prefixed, and seven were post-fixed. We do not look upon these figures as more than an indication of how this area may vary; for twenty cases are too few to form the basis of any statistical conclusions.

We believe, however, that the areas on the trunk are less liable to true variation than those on the limbs. Those which affect the terminations of the limbs are the most variable of all, but the infrequency with which they appear renders a more definite statement impossible.

It might be objected that the instances given above are not cases of variation but of false enumeration. This is rendered improbable by comparing the two cases in our series (Case 3 and Case 13) in which the *post-mortem* examination showed the 6th dorsal to have been affected. In Case 3, that of a child, the eruption (fig. 3) ran almost straight round the body, passing just below the angle of the scapula and below the nipple. In Case 13 on the other hand, the upper border of the eruption (fig. 13) touched the lower angle of the scapula and passed forward beneath the nipple, sending an upward tag to just implicate the lowest part of the areola. Yet in both these cases the *post-mortem* examination showed that the 6th dorsal was affected. Now the eruption in Case 3 followed what we should call the normal course; in Case 13 it was pre-fixed. Moreover, this eruption showed exactly the characteristics we laid down as necessary for a pre-fixed area, when discussing the variations in the 3rd dorsal; for it resembled the area above it, the 5th dorsal, in sending a branch to the nipple, and yet its upper border was distinctly lower than that of a normal 5th dorsal.

So far we have met with no case where an eruption that lay entirely over an area to which we had habitually given one number, turned out on *post-mortem* examination to have been due to an affection of the ganglion above or the ganglion below. That is to say, in each case where from examination of a previous case we had been led to suppose that the 3rd cervical, the 4th dorsal, the 7th dorsal, or the 12th dorsal would be affected, the enumeration again turned out to be correct.

Thus, in conclusion, we believe that when a certain ganglion is affected the eruption most frequently lies over a definite tract of skin, which may be called the normal area from which fibres enter that ganglion. This tract of skin may, however, in some cases be situated further headwards, and occupy about one-half or less of the area usually supplied by the segment in front (pre-fixed). It may also be situated further towards the tail end of the body, and occupy about one-half or less of the area usually supplied by the segment behind it (post-fixed). But its displacement never exceeds half an area in either direction, and in no case did we find that an eruption, which lay over what we supposed to be the complete normal area of a certain segment, was produced by a lesion of either the ganglion above or the ganglion below.

§ 4. *Overlap and Interdigitation.*—After what we have said in the preceding sections concerning the possibility of change in the shape of these segmental areas owing to individual differences in the shape of the patient's body or to actual variation of nerve-supply, it will at once be seen how difficult it is to determine to what extent these areas overlap. Thus in every case it becomes necessary to consider whether the area occupied by the eruption belongs to the normal type. If this be so we can then only determine the extent of the overlap by comparing it with the normal distribution of the area in front of it and the area behind it in a case where the body of the patient was of approximately the same shape. For it is useless to attempt to compare the 10th dorsal, however normal it may be, when spread out round the body of a baby, with the 9th dorsal around the small waist of a woman in the hope of determining to what extent these two segments overlap.

A third difficulty with which we have to deal is the extraordinary interdigitation of the serrated margins of these areas. They can rarely be defined by straight lines, for the eruption is made up of a series of outbursts, each of which follows the course of a tiny nerve-twig. Now it is quite impossible to say how far the downward tags of one area fit into the notches of the area below, but all we can say is that if the downward tag is a large one and forms an integral and distinctive feature of the area in its normal form, a notch of greater or less depth will be found in the area below corresponding, though not to the full extent, with this downward projection of the area above. (Compare the downward course of the posterior patch in fig. 5 with the notch in the upper border of the posterior patch of fig. 8 and fig. 4).

Let us then first compare the extent of the eruption in Case 2 or Case 9, which occupied the 7th dorsal area, with that of Case 16, that lay over the 8th dorsal. All these cases were men, and the rash in Case 2 was almost identical with that in case 9. It will be seen that the lower border of the area in figs. 2 and 9 scarcely encroaches at all on the upper border of that in fig. 16. Moreover, the apex of the anterior half of the eruption in fig. 16 fits into the notch made by the junction of the anterior with the posterior half of the area in figs. 2 and 9. In fact, the overlap does not consist of one-third of the extent of either of these areas. This slight overlap we believe to be typical of the areas of the trunk.

Turning next to the cervical region, fig. 6 shows a typical third cervical, and fig. 10 a fourth cervical with a rather extended anterior border, but a normal posterior border. In both cases the patients were men. It will be seen that the anterior or cephalic border of the fourth cervical (fig. 10), lies over the area occupied by the third cervical (fig. 6). But although these two areas habitually overlap, the extent of the overlap is not so great as might at first sight appear, for the third cervical runs in two main streams across the outer part of the supraclavicular fossa, and between these two streams the skin is affected either lightly or not at all. In the same way the anterior or cephalic portion of the fourth cervical (fig. 10), which also covers the outer part of the supraclavicular fossa, is always lightly marked both by erythema and vesicles in obvious contrast to that part which lies over the shoulder.

We believe that the overlap is more marked on the limbs, especially at their termination, but owing to the comparatively small number of cases on the fore-arm and leg (p. 394) it is impossible to be certain of the amount of this overlap.

Thus, in conclusion, the areas marked out by the eruption of herpes zoster overlap one another to a very variable extent. On the trunk this overlap is slight when individual differences and variation in nerve-supply are taken into account. In the neck this overlap consists more of a sharing of a certain territory than of true overlap, but on the limbs, especially at their termination, the overlapping is distinct.

Yet in no case does the zone of overlap equal in extent more than one-half of the area above and below, whilst in many cases it is considerably less.

Part III.

Case 1.—John William K., aged 64. Marylebone Infirmary (Mr. Lunn). Died February 23, 1897.

Summary.

No history obtainable.

Admitted for paraplegia. Paralysis extended as high as lower ribs on both sides. Cystitis and retention of urine.

Herpes appeared over the 1st lumbar area on the left side three days before death and continued to come out up to death.

Myelitis of the spinal cord as high as the upper dorsal region.

The 1st lumbar ganglion on the left side showed a large hæmorrhage in the centre with much surrounding infiltration by small round cells that stained deeply with Nissl's blue. The ganglion cells were destroyed, and those which remained failed to stain with Nissl's blue in the presence of a counter stain.

The remaining ganglia were normal.

The peripheral nerves showed no change.

Beyond marked degeneration of the vessels the brain showed no change.

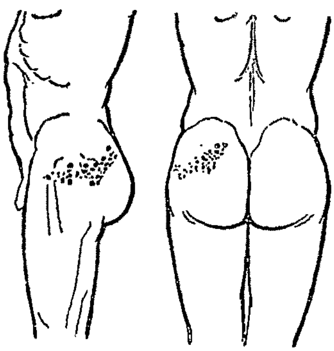

FIG. 1.

To show the distribution of the eruption in Case 1.

He was admitted to the infirmary on February 10, 1897, for paraplegia and complete incontinence of urine and fæces. He was completely paraplegic up to the level of the lower ribs and the abdominal muscles were paralysed. He was semi-comatose, with a temperature of 101·6° F. and sensation could not be tested. He was said to have incontinence of urine, but on admission his bladder was over-full and the incontinence appeared to be due to overflow.

On February 19 an herpetic eruption appeared over the area in fig. 1, and was still coming out when he died on February 23.

Thus the herpetic eruption began to appear three days before death.

POST-MORTEM EXAMINATION.

Made forty hours after death in cold weather. From a few hours after death until the examination the body lay upon its face surrounded by ice. It was found to be in excellent condition at the examination.

No bed sores.

Lungs showed much hypostatic congestion but there was no pneumonia. The substance of the heart was extremely soft and of a brown colour with marked striation. No valve lesion.

Spleen of normal size, but soft. Capsule of the kidneys stripped with fair ease and did not bring away the cortex. Cortex perhaps a little diminished. Liver normal.

The bladder showed marked thickening from old cystitis and the mucous membrane was of a purple-red colour.

Brain.—Arteries extremely degenerated and atheromatous, and in some places they were almost blocked by white clot. The cortex was well developed and showed no marked wasting. Membranes stripped easily and without decortication. Ventricles not distended nor granular. No hæmorrhage. No softening.

The lower portion of the cord was very soft and almost diffluent from myelitis.

MICROSCOPICAL EXAMINATION.

A microscopical examination was made of (*a*) a series of posterior root ganglia, (*b*) a series of peripheral nerves, (*c*) the spinal cord.

(*a*) *Ganglia.*

Dorsal 12, lumbar 1, 2, 3, 4, 5, of both sides were fixed in 96 per cent. alcohol and imbedded in paraffin. Sections were cut, mounted in strict series and stained by Nissl's method, Held's methylene blue and erythrosin, and with methylene blue and eosin.

Dorsal 12.—The vessels of the sheath of this ganglion on both sides were much engorged, but otherwise no gross change was present.

Lumbar 1. *Left.*—When the ganglia were completely hardened it was at once evident that this ganglion differed from its fellows. It was smaller, and at the same time much softer than any other ganglion of the series, and whereas the other ganglia were hard and resistent to the finger the 1st lumbar ganglion of the left side had the semi-fluid feel of an over-ripe gooseberry. It was therefore divided transversely across the centre with a sharp razor, and was then seen to contain a mass of soft pulpy material in the centre. The two halves were embedded and cut together so that the exposed surface corresponded to the incision through this soft central mass.

The following changes in an extreme form extend over forty sections. The centre of the ganglion is occupied by a large space with ragged edges. In sections taken from either end of the ganglion the centre is seen to be composed of effused blood more or less altered and surrounded and infiltrated with fibrin. Towards the periphery of this focus are a large number of small round cells which have stained deeply with methylene blue.

Amongst the débris in the centre no remains of ganglion cells or normal ganglionic structure can be seen, but in the peripheral layers broken down ganglion cells can be seen, staining in some cases a rich golden colour. The contrast between these ganglion cells and the small round cells, with their deep blue staining, is marked. Between the focus of destruction in the centre and the ganglionic sheath are many ganglion cells which have stained pink with erythrosin or remained pale.

Thus the centre of this ganglion is occupied by a large hæmorrhage which had completely destroyed it, whilst around this central focus lie ganglion cells that were either dead or markedly altered in vitality before the death of the patient. Moreover, the whole of the ganglion around the central focus of destruction is filled with small round cells that stain deeply with methylene blue.

At the level where this change is best marked the anterior root is seen as a compact bundle lying in its own subdivision of the ganglionic sheath.

The sheath of the ganglion shows no thickening and no marked alteration of any kind.

Lumbar 1. *Right.*—The cells of this ganglion do not stain well with Nissl's blue, but there is no hæmorrhage and no infiltration with small round cells. The central vessel is well seen and contrasts well with the hæmorrhagic focus in a similar position in the ganglion of the left side.

Lumbar 2.—Neither right nor left ganglion show any marked change.

Lumbar 3 *and* 4.—None of these ganglia show any change.

(*b*) *Peripheral Nerves.*

The peripheral branches of the 12th dorsal, 1st, 2nd, and 3rd lumbar were stained by Marchi's method and examined in teased specimens and by sections, but no change was found.

(*c*) *Spinal Cord.*

As high as the upper dorsal region the whole area between the posterior horns was markedly destroyed. The vessels appeared to be plugged with clot of some standing, and the posterior columns were converted into a mass of débris consisting of broken-down fibres and a large number of small round cells, apparently leucocytes.

In the mid-dorsal region this disintegration extends in an irregular manner into the lateral columns. Thus the cord showed myelitis mainly affecting the posterior columns, but also invading to a less degree other portions of the cord as high as the upper dorsal region.

Above this no change is seen except the universal thickening of the walls of the vessels of the pia arachnoid.

Case 2.—James T., aged 35. Admitted to the London Hospital October 31, 1899. Died November 2, 1899.

SUMMARY.

A case of aortic obstruction and regurgitation. Admitted for cardiac failure with swelling of legs. Death followed two days after admission.

An extremely severe herpetic eruption was present over the area in fig. 2 corresponding to the 7th dorsal segment. It had begun to appear seven days before admission or nine days before death.

Microscopically, the 7th dorsal ganglion on the right side was found to be profoundly affected. The whole ganglion was infiltrated with small round cells and more than half the ganglion was riddled with extravasated blood. (*Plate* 1, *fig.* 1.)

The peripheral nerve trunk for nearly 2 cm. from the ganglion showed profound inflammatory changes with an effusion of blood into the centre of the swollen nerve, changes identical with those in the ganglion.

The 5th, 6th, 8th, and 9th dorsal posterior root ganglia and the 7th dorsal ganglion of the left side were normal.

No secondary degenerative changes were found in the posterior roots or spinal cord.

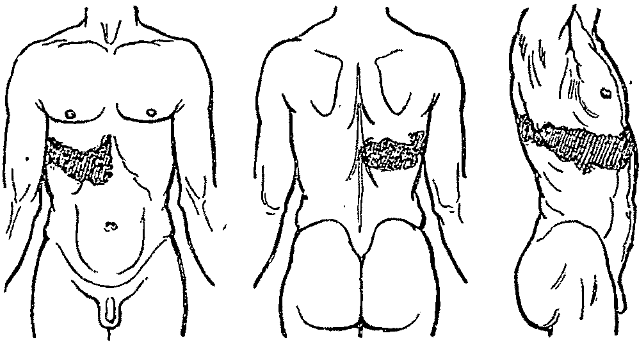

FIG. 2.

To show the distribution of the eruption in Case 2.

History.—His speech has been husky for two years and he has had cough and increasing weakness for one year. On November 1, 1898, he was seized with pain over the heart which lasted for three hours. He then slept for two hours and woke without pain, but with dyspnœa which prevented his lying down for three or four days. Since that time he has had frequent attacks of a similar kind. For the last eight weeks his legs have been swollen and he has been obliged to sleep in a chair for more than a week.

There is no history of rheumatism in any form, but he admits syphilis.

On admission he was extremely ill and lay propped up in bed with head thrown back on his pillows. His face was a little puffy and his legs and thighs œdematous. There was an extremely marked and severe herpetic eruption on the right side over the area in fig. 2 corresponding to the 7th dorsal. It had first appeared on October 24, and had now reached its full development.

He suffered from no pain, but had dyspnœa with a short cough at times. The sputum was muco-purulent.

Cardiac impulse heaving, diffuse and fairly regular, situated in the 6th intercostal space. An aortic systolic and diastolic murmur was audible, but there appeared to be no mitral systolic murmur.

There was dulness with absence of breath sounds and vocal resonance over the left base.

The urine contained one-fifth albumen.

Progress.—On the evening of November 1 he had a severe cardiac attack during which his pulse became irregular. He rallied somewhat after venesection, but died in the early morning of November 2, nine days after the appearance of the herpetic eruption.

POST-MORTEM EXAMINATION.

Eight hours after death, in cold weather.

The right pleura contained two pints of clear fluid; the left was obliterated by old adhesions. Both lungs were emphysematous and congested. The left base was infiltrated with bronchopneumonic patches to such an extent that portions of the lung sank in water.

The heart weighed 16½ oz. (467 grammes). Both sides were much enlarged. The left ventricle was dilated but not much hypertrophied, and parts of its wall were markedly fibrous. The right ventricle was dilated and its wall was hypertrophied. The aortic valves were much thickened and puckered, especially at the attached and free margins. The mitral valve was slightly thickened and admitted three fingers easily. Pulmonary and tricuspid valves normal. There was extreme atheroma of the aorta.

The spleen weighed 7½ oz. (212 grammes). The kidneys contained one or two small cysts and the capsule was slightly adherent. The cortex when stripped was a little irregular. They were of normal size. The liver weighed 4 lb. 3 oz. (1899 grammes) and was slightly fatty.

The brain was normal in colour and size. Its arteries were tough, but showed no nodular thickening. The membranes were normal and stripped well. Pons, cerebellum, medulla, and cord normal to the naked eye.

MICROSCOPIC EXAMINATION.

A microscopic examination was made of (*a*) a series of posterior root ganglia, (*b*) a series of nerve roots, (*c*) a series of peripheral nerves, (*d*) the spinal cord, (*e*) the skin within the herpetic area, (*f*) certain lymphatic glands.

(*a*) *Posterior Spinal Ganglia.*

The 5th, 6th, 7th, 8th, and 9th root ganglia were dissected out and hardened for four hours in corrosive sublimate, washed in running water for sixteen hours, and placed in 30 per cent. spirit. From this strength they were gradually carried up to absolute alcohol. They were then embedded in celloidin and cut in series of longitudinal sections.

Dorsal 7. *Right.*—When the 7th dorsal ganglion of the right side was dissected out it was at once obvious to the naked eye that it was different from its fellows. It was not reddened but looked swollen. Moreover, that portion of the peripheral nerve close to the ganglion was obviously swollen, being for a short distance nearly as thick as the ganglion itself. This portion was hardened and embedded with the ganglion and cut longitudinally.

Microscopically (plate 1, fig. 1), the early sections, which include the sheath only, show extremely marked engorgement of the vessels, and over the swollen portion of the peripheral nerve blood seems in places to have escaped from the vessels. The sections through the ganglionic substance itself show three well-marked changes. Firstly, there is a great increase of small round cells which lie packed in thick clumps between the ganglion cells. These cells stain well with methylene blue. Secondly, the whole of that half of the ganglion on the side opposed to the anterior root bundle is honeycombed with small hæmorrhages. Long streaks of extravasated blood run almost parallel to the contour of the capsule, and multitudes of small hæmorrhages dot the substance of the ganglion. Thirdly, wherever the small round-celled infiltration is marked, and in the neighbourhood of each hæmorrhagic spot, the ganglion cells have undergone a profound change. If a nerve-cell lies in the centre of a hæmorrhage it does not stain at all with methylene blue, and in specimens prepared by the Nissl method appears as a white ghost. Such cells, however, stain readily with eosin or saffranin. If these cells are examined under a high power they are seen to be broken up into fine globular masses, and here and there they are eroded by leucocytes that have invaded their capsule. There is no vacuolation or extrusion of nuclei. The cells have the appearance of a tissue that has been suddenly killed. On the other hand, in those parts of the ganglion which contain no hæmorrhages but are infiltrated with small round cells, the ganglion cells are seen under a low power to stain fairly well, but under a high power they present a ground-glass appearance with some reduction of Nissl bodies, but no vacuolation or alteration in the nuclei. Thus, considering that the ganglia were hardened in corrosive sublimate, these cells cannot be said to show any marked change; for the appearances obtained in posterior root ganglion cells with this fixative differ from those that follow alcohol hardening, although in themselves they are equally constant and characteristic.

Left.—This ganglion is normal and shows none of the changes present in that of the right side.

Dorsal 5, 6 *and* 8. *Right and left.*—All normal.

(*b*) *Posterior Nerve-roots.*

The 5th, 6th, 7th, 8th, and 9th dorsal roots of both sides were stained by Marchi's method. In no case could any definite signs of acute degeneration be discovered. The 6th and 7th dorsal roots on both sides were stained by Stroebe's method (after treatment by Marchi's method), and no change could be discovered.

(*c*) *Peripheral Nerves.*

Rather more than 1 cm. of the peripheral nerve of the 7th dorsal on the right side remained attached to the ganglion, and was hardened, cut, and stained with that structure (*vide supra*). It showed signs of inflammation and hæmorrhage, exactly resembling the changes seen in the ganglion.

The posterior primary division and the anterior trunk of the 6th, 7th, and 8th nerves on both sides were treated by Marchi's method. No change could be discovered.

(*d*) *Spinal Cord.*

The spinal cord was hardened in Müller's fluid, and every segment above the 9th dorsal was cut in celloidin. No change of any kind was discovered.

(*e*) *The Skin within the Area covered by the Eruption.*

Portions of skin on which the eruption was still well marked at death were hardened in a saturated solution of corrosive sublimate and cut in the usual manner. They were stained for micro-organisms, but without result. Moreover, inoculations were made from the vesicles on many different media, but in every case they remained sterile. These observations were kindly made for us by Dr. Bulloch, bacteriologist to the London Hospital.

Sections through an unruptured vesicle show a cavity, the floor of which is formed by naked papillæ. These papillæ, in a condition of profound inflammation, are infiltrated with masses of small round cells, which stain deeply. This infiltration with small round cells extends to the termination of the hair follicles and of the sweat glands. Here and there small collections of deeply-staining round cells are seen even in the deeper layers of the skin, apart from either sweat glands or hair follicles.

The vesicle is split up into incomplete cavities by irregular septa extending from the roof to the floor. These septa are evidently the remains of incompletely-severed epithelial layers. The cavity is filled with a fluid that has coagulated into a somewhat granular hyaline mass under the influence of the hardening agent. Within this mass lie small round deeply-staining cells and broken-down epithelial cells of all sizes and shapes, which have lost their prickles. In this case we were unable to see any of the large polynuclear cells not infrequently found in such vesicles.

(*f*) *Axillary Lymphatic Glands.*

It was noticed during life that the glands lying under the posterior border of the pectoralis and in the summit of the axilla were enlarged and tender. They were therefore incised two hours after death with rigid aseptic precautions, and cultivations were made from them by Dr. Bulloch. They were uniformly sterile.

The glands were removed and hardened in corrosive sublimate. Sections showed no micro-organisms.

Yet these same sections showed that the glands were in a condition of profound inflammation. Foci of small round-celled inflammation are scattered throughout, not only the glandular portion, but also throughout the trabeculæ.

Case 3.—John K., aged 5. Admitted to Guy's Hospital, April 9, 1897. Died April 21, 1897 (Dr. Pye-Smith).

SUMMARY.

Admitted for acute bronchitis. Herpes zoster appeared on April 11 *over the area in fig.* 3 (*dorsal* 6). *Death eleven days after from tubercular broncho-pneumonia and miliary tuberculosis. Acutely degenerated fibres were seen to enter the cord by the* 6*th dorsal root on the right side. This degeneration extended up in the posterior column as high as the level of entry of the* 2*nd dorsal root.*

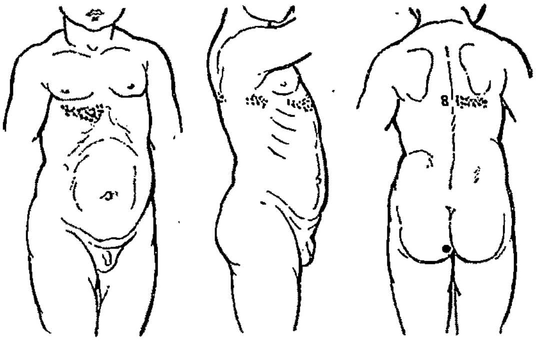

FIG. 3.

To show the distribution of the eruption in Case 3.

On admission the patient was a small fair boy in fairly good condition, and with no evidence of rickets. His temperature was 101°.

Respiration 30. Much dyspnœa and cyanosis. Mucous râles heard all over the chest.

Pulse 156, small and irregular. Heart sounds faintly heard.

Urine acid; contains no albumen or sugar.

April 11. Herpes zoster has appeared occupying an area behind corresponding to the eighth rib, whilst in front the eruption is situated over the fifth and sixth intercostal spaces. In the axillà is a third (lateral) patch situated on the horizontal level of a line joining the anterior or posterior patches (fig. 3).

April 21. Died at 8.30 p.m.

POST-MORTEM EXAMINATION.

The bronchial glands were caseous, and one of considerable size was adherent to the left bronchus. Tubercles were scattered throughout the lungs, and some tubercular foci had begun to caseate. Both bases were collapsed, and showed in addition patches of broncho-pneumonia.

Heart normal.

Spleen was enlarged and contained tubercles of various sizes on its surface and throughout its substance.

Kidney contained a few tubercles.

Liver weighed 794 grammes. Tubercles seen on its surface. A little recent capsulitis.

The spinal cord was removed, but as neither of us was present at the *post mortem*, unfortunately no ganglia were dissected out. The spinal cord was preserved in Müller's fluid and passed into the hands of one of us a few days later.

MICROSCOPICAL EXAMINATION.

The spinal cord was divided into segments corresponding to the entry of the various nerve-roots, and each segment was stained by Marchi's method. Beginning below and examining segment by segment, no abnormality is seen until the level of upper part of the entry of the 7th dorsal root is reached. At this level a few scattered black dots are seen, not in the entering root, but in the root zone of the postero-external column. These black dots are sparse and much scattered, and the appearance in no way resembles that seen in the next segment above (plate 2, fig. 2).

With the extreme lower fibres of the 6th dorsal root on the right side a mass of black fibres are seen to enter and to spread out in the right posterior root zone (plate 14, fig. 2). The left side shows no black dots whatever, and the specimen is a particularly clean Marchi preparation, without any diffuse black dots so often seen in less successful preparations. Degenerated fibres can be seen to enter the cord by the 6th root on the right side as far up as the entry of the extreme upper fibres of this root.

Throughout this part of the cord opposite the entry of the 5th root the degenerated fibres are seen to lie partly in the posterior horn and partly in the root zone. In the segment opposite the 4th root they have left the posterior horn and lie entirely in the root zone, leaving the entering root and posterior horn free from black. They steadily decrease in number, and at the level of the entry of dorsal 2 would easily be missed had they not been traced from below.

(At this point the cord had been injured so that the upper part of dorsal 2, and the whole of dorsal 1 were unavailable for examination.)

Cervical 8, and all the segments above up to the top of the cord were absolutely free from any signs of degeneration.

Case 4.—Elizabeth V., aged 58. Admitted to Rainhill Asylum on August 23, 1860. Died July 5, 1900.

SUMMARY.

On June 22, 1900, *an imbecile patient developed a profound herpetic eruption over the area in fig.* 4, *corresponding to dorsal* 12. *She died from an undetermined cause thirteen days later.*

Post-mortem *examination revealed no naked-eye disease in the nervous system except that the* 12*th dorsal nerve of the left side could be seen to be swollen in the neighbourhood of the ganglion; but on microscopical examination the following changes were found:*

(*a*) *There was an extreme necrotic lesion in the* 12*th dorsal ganglion of the left side, probably of vascular origin. This caused disintegration of three-fourths of the body of the ganglion.*

(b) The 12th dorsal posterior root was profoundly degenerated on the left side. The 1st lumbar root on the same side also showed a few degenerated fibres.

(c) Both posterior and anterior primary divisions of the mixed nerve peripheral to the 12th dorsal ganglion on the left side showed profound degenerative changes.

(d) Degenerated fibres entered the spinal cord on the left side at the level of the 12th dorsal root. This degeneration, which appeared to have not yet reached its height, could be traced up in the posterior columns as high as the 5th cervical segment.

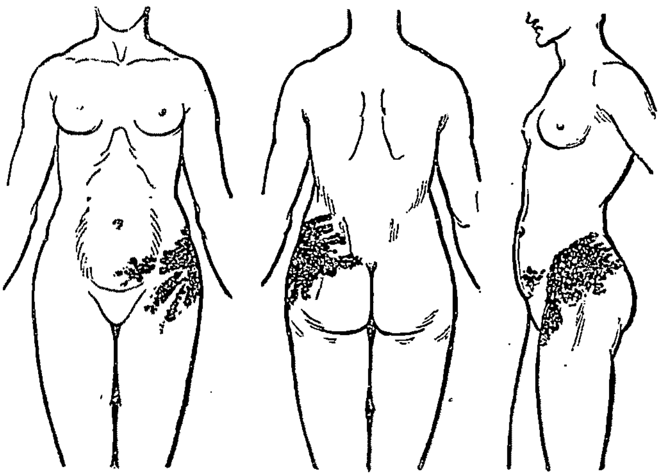

FIG. 4.

To show the distribution of the severe eruption in Case 4.

History.—The record of her forty years of confinement in Rainhill Asylum contains few facts of interest. She was admitted at the age of 18 and was then classified as an imbecile. For the past fifteen years she remained in a state of almost complete dementia, dull, inattentive and unobservant, incapable of entering into conversation or engaging in any employment. She was always untidy in person and dirty in her habits.

Though of delicate constitution and in feeble condition an occasional attack of diarrhœa is the only illness from which she is reported to have suffered.

On June 22, 1900, an herpetic eruption accompanied by marked erythema appeared over the gluteal region of the left side. Fig. 4 is reproduced from some extremely careful drawings, to a scale of one-half life size, by Mr. Marriott, to whom our best thanks are due. At the same time the eruption was seen by one of us and was found to correspond exactly with the drawings.

The eruption had the following distribution. Viewed from behind it was seen to slope over the lateral aspect of the buttock.

There were two or three insignificant, isolated vesicles between the main eruption and the middle line, but the roughly serrated and very irregular inner margin of the concrete portion did not reach quite half way across towards the middle line, and the upper portion lay further outwards than the lower. The upper border was of convex shape and its summit was placed in the flank about one inch (2·5 cm.) above the crest of the ilium. The lower border sloped from behind downwards and forwards, following a line drawn between the posterior-superior spine of the ilium and the great trochanter.

From the lateral aspect a more comprehensive view of the eruption was obtained. The upper border was again situated about one inch (2·5 cm.) above the ilium and ran almost parallel with the crest of that bone. The lower border still sloped down in a straight line and was continued on to the upper part of the thigh in front of the great trochanter. The lower portion of the eruption as seen from the side had a patchy appearance, owing to the presence of islets of healthy skin.

From the front the eruption had a curious distribution difficult to describe. In the hypogastric region was a patch of considerable size connected with the main eruption by a narrow neck; the upper margin of this patch ran transversely slightly below the level of the anterior-superior spines of the iliac bones. The inner border, which dropped more or less vertically downwards, lay from one and a half to two inches (4 to 5 cm.) to the left side of the middle line. Its lower border sloped downwards almost parallel to Poupart's ligament and joined the inner border immediately above the mons veneris.

Lastly, from the lower part of the main eruption two pointed streamers were seen running down the upper part of the front of the thigh parallel to Poupart's ligament. The lower of these two projections consisted almost entirely of erythema.

Along the crest of the ilium the vesicles were largest and most numerous. As the patient could not refrain or be prevented from scratching the eruption it rapidly became worse, and in the course of a few days the entire area had assumed an impetiginous character. Finally pustulation ceased, and healthy granulations formed.

She was kept in bed during the whole of this period, and no change was noted in her general physical condition; but on July 5, thirteen days subsequent to the appearance of the eruption, she suddenly collapsed, her limbs became rigid, and she died in two hours' time.

A specimen of urine collected immediately prior to death was found to be loaded with albumen.

POST-MORTEM EXAMINATION.

The examination was made twenty-two hours after death.

The cadaver was thin, almost emaciated.

Owing to the supervention of acute inflammatory hæmorrhagic changes, the area of skin over which the herpetic eruption was previously distributed could be defined with the greatest distinctness; the cutis was shed, the surface excoriated, and the whole area had the colour and appearance of raw beef steak. The subcutaneous tissues in this region were also somewhat brawny and œdematous.

No other sign of skin disease was noticed.

Head.—The scalp was thickly covered with hair. With the exception of some increase in density the cranial bones were free from abnormality. The dura mater and its venous sinuses were also healthy. There was some excess of subdural fluid, but no blood or membrane formation. The pia-arachnoid membrane was slightly thicker than normal, but was not unduly adherent. The pial vessels generally were slightly engorged with blood, and the larger arteries at the base of the brain exhibited signs of early atheroma.

The encephalon, though small, was of perfect shape. The convolutions in general were slightly wasted, but entirely free from gross or focal lesion of any sort; their disposition followed a simple type.

The cerebral cortex was rather dark in colour, moderately hyperæmic, and slightly reduced in depth.

The lateral ventricles were somewhat dilated and contained a correspondingly increased amount of fluid.

The condition of the white matter, basal nuclei, &c., calls for no remark. Also the cerebellum, pons, &c., showed no change worth noting.

Spine.—No naked-eye change was observed in the spinal cord or in any of the series of posterior root ganglia and peripheral nerves which were extracted for microscopic examination.

It must here be mentioned that careful examination proved the existence of only eleven pairs of ribs, the lowermost pair being absent. The discovery of this abnormality prevented a mistake in the enumeration of nerves and ganglia which might have occurred if the last pair of ribs had been taken as the only guide.

Thorax.—The chest was of small size and the ribs slender and easily broken, but there were no pleural adhesions and the lungs were in a healthy condition.

The heart muscle appeared to be rather paler and softer than usual, but the organ was of normal size and shape and free from valvular lesion. The aorta also was not obviously atheromatous.

Abdomen.—The peritoneum was in a normal state.

The liver substance was rather soft. The gall-bladder contained about three dozen stones, having an average diameter of 3 mm.; some were smooth and round, while others were faceted. All were of a grayish-yellow colour externally and had a dark brown core.

The spleen was healthy.

The capsule of the kidneys stripped cleanly and the cortex and medulla were of normal relative depth, but the cortex was pale and the substance in general congested; it was not, however, obviously cirrhotic.

The bladder was moderately distended and contained high-coloured urine.

The alimentary tract and the uterus, &c., were normal.

The following weights were recorded: encephalon, 1,185 grammes; right hemisphere, unstripped, 495 grammes, stripped, 462 grammes; left hemisphere, 500 grammes; cerebellum, pons, and medulla, 160 grammes; right lung, 10¾ oz. (304 grammes); left lung, 9 oz. (254 grammes); heart, 7½ oz. (212 grammes); liver, 35 oz. (990 grammes); spleen, 2 oz. (56 grammes); right kidney, 3½ oz. (99 grammes); left kidney, 3½ oz. (99 grammes).

MICROSCOPIC EXAMINATION.

(a) *Posterior Root Ganglia.*

The ganglia were fixed in 5 per cent. formalin, and after treatment with alcohol were embedded in paraffin and cut serially in longitudinal sections. Some sections were stained with thionin, others by the method of van Gieson, and others with hæmatoxylin alone.

Dorsal 12. *Left.*—This ganglion is the seat of most important changes (plate 8, figs. 3 and 4). We will begin by describing the appearances seen in sections from about the middle of the ganglion, for here the changes are most obvious. The ganglion is so cut that it here appears as an oval body, to which at one end a portion of the posterior root, at the other a portion of the peripheral nerve, are attached, whilst the anterior root is cut in its long axis and lies closely approximated to the less convex side of the oval ganglion.

The whole ganglion is gravely diseased with the exception of about one quarter of the field that lies in close apposition to the anterior root.

The nerve cells in this diseased area are swollen and seem to distend the surrounding capsule.[1] Their nuclei are likewise swollen, and in thionin specimens stain of a uniform blue colour, which is so intense that no nucleolus and no trace of the normal delicate reticular arrangement of the nuclear substance is recognisable. Further they retain their colour so firmly that they are still plainly evident even when decolorisation and differentiation are carried to an extreme extent and most other structures have given up the dye. In van Gieson preparations these nuclei appear of a dark brown colour, and with Ehrlich's hæmatoxylin they assume a uniform deep purple.

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[1] In a specimen of a posterior root ganglion which has been fixed in perchloride of mercury and carefully prepared, the nerve-cells will be found to completely fill the investing capsule, and this we may regard as the normal condition; but in specimens fixed in formol, it is our experience that a certain amount of shrinkage occurs, and owing to retraction, the cell is attached to the sheath in places only, its periphery is jagged and spaces are left between it and the capsule. The latter condition we have noted in cells lying in the healthy portion of this ganglion and also in cells of other ganglia from the same case which we have examined for control purposes, and therefore the statement that the cells in the diseased area "seem to distend the surrounding capsule," seems justifiable.

We would mention that we employ formol for the fixation of tissues such as ganglia, because it allows us to display the condition of both nerve-cells and nerve-fibres in the one piece of tissue, which is often desirable. Alcohol and perchloride of mercury, of course, do not possess this advantage.

This intensely chromophilic condition of the nuclei, in addition to being a most prominent feature of these cells, is also of importance in so far as it affords a clue to the genesis of the ganglionic lesion in cases of herpes zoster, for we have noticed in cases of cerebral embolism or thrombosis in which the subsequent process of softening and disintegration has not proceeded so far as to preclude the possibility of a microscopic examination, that a precisely similar condition of the nerve-cells has existed, and as we shall presently indicate, there are other changes observable in this ganglion which favour the assumption that the primary cause of the lesion is of the nature of an interruption or obliteration of the local vascular supply.

In regard to the bodies of these cells, the substance has a uniformly blurred appearance entirely devoid of definite structure, and the chromophilic particles of Nissl are completely obscured. The particles of pigment normally pertaining to the cell body remain, but they are altered in position; thus in the larger cells this pigment, instead of lying at one end of the cell close to the margin, tends to be arranged in the form of a halo or crescent round the nucleus, and is separated from the periphery on the one hand and from the nucleus on the other by a distinct space. In the van Gieson and hæmatoxylin preparations the substance composing the bodies of these cells has also a blurred look.

Turning next to the condition of the supporting or ground substance of this area, its chief characteristic is that it is blurred; that is to say it stains badly and more or less homogeneously. For instance, in the van Gieson specimens, the red blood-corpuscles are of a grayish-brown colour, whereas in the normal condition they stain a vivid yellow or pale pink; then the nuclear elements which should be present in abundance, stain of a purple colour and be sharply defined, are on the contrary few in number, blurred and indefinite in outline and of a grayish-brown colour. But in spite of the defective stainingthe existence of extravasated red blood-corpuscles can be readily recognised evenly distributed over the whole area and not collected into large masses.

The strands of nerve-fibres passing through the ganglion are plainly seen. They stain a pale pink tint by van Gieson's method, and the primitive sheaths and axis cylinders absorb most of the colour, and the latter are distinctly swollen. All these fibres give the impression that they are undergoing an acute degenerative change.

The periganglionic sheath covering the diseased area does not seem to be specially thickened, nor infiltrated with small round cells, nor are there any hæmorrhages in it.

Coming now to that part of the ganglionic substance lying adjacent to the anterior root which has been alluded to as approximately normal, all the constituent elements stain perfectly well by the various methods. Thus in the nerve-cells a deep-stained nucleolus and a pale nucleus with its delicate reticular network is recognisable, the chromophilic elements of Nissl are clearly defined, and the pigment is normally disposed. The nuclei of the supporting tissue stand out clearly. Here the structure of the walls of the blood-vessels can be plainly defined. The corpuscles contained in these vessels stain normally, but every vessel is engorged with red blood-corpuscles, leucocytes are unduly abundant in their neighbourhood, and in many places extravasations have occurred.

This intense hyperæmia is undoubtedly a pathological condition, and cannot be ascribed to *post-mortem* hypostasis. It resembles the zone of hyperæmia investing an embolic infarct in a kidney.

The remaining serial sections of the ganglion show that the area which has undergone disintegration is sharply circumscribed and involves fully three-quarters of the substance of the body of the ganglion.

It must next be mentioned that the hyperæmic and hœmorrhagic condition described above is not confined to the ganglion, for on examining the attached portion of the peripheral nerve one finds that an extensive pouring out of blood has occurred in the centre of the bundle; lines of effused red blood-corpuscles separate the strands of nerve fibres from one another, and these, along with numbers of engorged blood-vessels, can be followed along it for a distance of several millimeters, continuous with the hæmorrhage in the ganglion. This hæmorrhagic area was noticed with the naked eye before the ganglion was imbedded, and in transverse section had a diameter of about 1 millimeter.

As the parts are so disorganised by hæmorrhage it is difficult to fix on any individual arteriole in this situation, an occlusion of which one might regard as the starting point of the mischief; but entering the distal end of the ganglion and proceeding into the centre of the diseased area already noted, is an artery of fairly large size which is suspicious in appearance, for instead of being congested, as all the other vessels are, it is quite empty, and there is also an excess of leucocytes along its wall.

Lastly, in the portion of the posterior root shown in these sections are more hæmorrhages and engorged vessels, but the anterior root is apparently free from such change, although the large artery which accompanies it is somewhat full of blood.

Dorsal 12, *left; Dorsal* 10 *and* 11, *right and left; Lumbar* 1 *and* 2, *right and left.*—These ganglia are all free from noteworthy alteration.

(*b*) *Posterior Spinal Nerve-roots.*

The posterior roots of both sides, from dorsal 11 to lumbar 2 inclusive, were stained by Orr's modification of Marchi's method (osmic acid 2 per cent. 4 parts, acetic acid 1 per cent. 1 part). They were then dissected out into their component twigs and one by one carefully teased and mounted in glycerine. We can confidently recommend this method for displaying degeneration in the spinal roots, because by it the condition of every fibre contained therein can be definitely ascertained.

Dorsal 12. *Left.*—As was expected, this root shows pronounced changes (plate 16, fig. 1).

It enters the cord in four twigs. In the first or uppermost twig fibres showing acute degenerative changes occur abundantly. To begin with, some are swollen and broken up into irregular beads or segments, each segment consisting of a ring of dark brown medullated substance which may be empty or may contain dark or pale round nuclei. On following along such a beaded fibre, one or more blackened clumps of myelin will generally be found in its course. Such fibres are probably in an early stage of degeneration.

In the next place, fibres are present which, although they possess a regular outline, are swollen in some lengths and contracted in others, their groundwork also stains more palely than that of the normal fibre, and in addition, distributed along their course and contained within the outer sheath, blackened globules of altered myelin occur; it is common to see these globules arranged in the form of large round or oval beads, but occasionally they occur as collections of small circular masses. Between these globules the substance of the nerve is in places strewn with coarse, highly refractile, pale brown particles; these are not unlike pigmented bodies, and they give a granular appearance to the portion of the fibre which they occupy. Such fibres as that last described are extremely common and probably represent a more mature stage of degeneration.

The remaining three twigs show similar changes, and an excess of fibrous tissue is manifest in none.

Dorsal 12. *Right.*—One glance at the preparations of this root suffices to prove that they are entirely different from those of the left side.

Careful search under a high power does show an isolated degenerated fibre here and there, but there are not more than ten altogether, and these are of no importance and are commonly found in Marchi preparations when there is no reason to suppose gross disease to be present. The remainder of the fibres are quite normal, their investing ring of myelin running in the form of a straight tube and being interrupted only at the nodes of Ranvier.

Dorsal 11. *Right and left.*—Careful teasing and searching examination only shows a few isolated degenerated fibres, and there is no excess of connective tissue.

Lumbar 1. *Right and left.*—There is again an isolated degenerated fibre here and there.

Lumbar 2. *Right and left.*—No changes of consequence.

Transverse and longitudinal sections of the above roots cut in paraffin afford confirmatory evidence of the above statements.

(*c*) *Peripheral Nerves.*

The peripheral branches of the 11th and 12th dorsal and the 1st and 2nd lumbar on both sides were stained by Orr's modification of Marchi's method. Some portions were teased and mounted in glycerine, whilst other portions were cut in paraffin both transversely and longitudinally.

Dorsal 12. *Left.*—The nerve is composed of two branches, one small one proceeding posteriorly, and another of larger size passing anteriorly. Both divisions show pronounced and important degenerative changes of an acute nature.

The small posterior division is most severely affected, and very few fibres can be discovered in it which appear to be in a normal condition.

Fibres possessing the following characters, all indicative of degeneration, are extremely common, and go to form the main bulk of the bundle. The normal cylinder of medullated substance is untraceable, and has been replaced by collections of black or dark brown globules; the groundwork stains of a pale-gray colour, and in it are distributed crowds of coarse, circular, refractile dark brown granules which occasionally occur in lines or fusiform clumps; swollen in some places, contracted in others, these fibres have a wavy outline. A few fibres are present in which the myelin sheath is swollen, beaded, and broken up into large oval or circular segments. Following such a fibre along, some clumps of blackened myelin, arranged in the form of beads, can generally be recognised in some parts of its course.

The anterior primary division of this nerve contains considerably more healthy fibres, but at the same time degenerated fibres are numerous. The pale-stained coarsely granular fibres are not so numerous as in the posterior primary division, but the segmented fibres and fibres in which the blackened masses of myelin have run into beads are more frequent.

These changes in the nerve-fibres were all noted in the teased preparations. Examination of sections, both transverse and longitudinal, affords confirmatory evidence of their existence, and shows further that the capillary blood-vessels which course in the endoneurium of these nerves are greatly distended, and have in many instances ruptured, so that the blood has poured out and separated individual nerve-fibres from one another.

After carefully comparing the preparations of this peripheral nerve with those of the corresponding posterior spinal nerve-root, it may be definitely stated that histologically the changes in the nerve-fibres of both structures are identical in character if different in degree.

Dorsal 12. *Right.*—A fibre here and there shows doubtful signs of degeneration, but on the whole it is healthy, and certainly entirely different from the corresponding nerve of the opposite side.

Dorsal 11. *Left.*—There are a few, perhaps eight or ten, degenerated fibres.

Dorsal 11. *Right.*—A good specimen of a degenerated fibre is not to be found. Along the course of many fibres an isolated black globule is here and there recognised; it is to be noted, however, that these globules never lie in the substance of the fibre, but always on the surface between the primitive and medullary sheaths, and occasionally they occur opposite to the nodes of Ranvier.

Lumbar 1. *Left.*—There is no doubt that a considerable number of fibres are degenerated, but such fibres are infinitely less numerous than they are in the 12th dorsal nerve of the same side. The degeneration is indicated by black beads or globules running along the course of the fibres.

Lumbar 1. *Right.*—In this nerve degenerated fibres are extremely scarce.

(*d*) *Spinal Cord.*

Method of examination.—Stained by Orr's modification of the method of Marchi, and cut transversely in paraffin (plate 12, fig. 1).

Dorsal 12.—Sections from the lower end of the segment show a few scattered degenerated fibres in the dorsal half of the postero-external column of the left side, but no diseased posterior root-fibres on the point of entry. At the middle of the block a few entering degenerated fibres are noticed. At the upper end of the segment a considerable number of fibres have entered and taken up a position along the inner margin of the left posterior cornu in its dorsal two-fifths, and other degenerated fibres are still passing in through Lissauer's tract.

Though the existence of this degeneration is unmistakable and the contrast between the two sides very marked, yet it does not seem to have quite reached maturity, for many fibres, though swollen and otherwise altered, do not give the black reaction with osmic acid, and on that account the diseased field is not so obvious as it probably would have become had a somewhat longer period elapsed between the outbreak of the eruption and death.

Lastly, it must be noted that the substance of the left posterior cornu immediately ventral to the substantia gelatinosa Rolandi is dotted with degenerated fibres. There is no degeneration whatever in any other part of the section, and no evidence of meningitis or any other disease.

Dorsal 11.—Few or no degenerated posterior root-fibres enter at this level.

Hugging the inner margin of the left posterior cornu in its dorsal half, but scarce at the periphery, is a distinct collection of degenerated fibres which from their position we can safely assume entered at dorsal 12. The degenerated fibres seen in the substance of the posterior horn of the left side are still present.

The right posterior column is normal, and the same remark applies to the rest of the field.

Dorsal 10.—The degeneration is beginning to leave the vicinity of the posterior cornu, but still touches it at the innermost part of the field.

Dorsal 9.—The degeneration is removed still further inwards, and has now assumed the form of a thin strip extending from the periphery to a point on the inner margin of the cornu opposite to the column of Clarke.

Dorsal 8 *and* 7.—Similar to dorsal 9.

Dorsal 6.—The degeneration occurs as a faint strip lying nearer to the posterior cornu than to the posterior median septum, and extending from the periphery inwards almost as far as the posterior commissure.

Dorsal 5.—Similar to dorsal 6.

Dorsal 4.—The degeneration is gradually approaching the middle line.

Dorsal 3.—The diseased fibres are becoming difficult to trace. At the periphery they lie about midway between the posterior median septum and the tip of the posterior horn, and from there they extend forwards to the middle of the posterior commissure.

Dorsal 2.—Similar to dorsal 3.

Dorsal 1 *and cervical* 8.—The degeneration is still traceable.

Cervical 7.—Some of these sections are particularly good ones and the degeneration is plainly seen in them; it first follows the septum which divides the column of Goll from the column of Burdach, and then, joining the posterior median septum, it proceeds along it down to the posterior commissure.

In cervical 6 *and* 5 a few blackened fibres can be recognised lying alongside the left postero-lateral septum, but above this the degeneration cannot be followed.

Lumbar 1.—No degenerated fibres enter the posterior columns at this level. Just a few blackened fibres are visible in the dorsal two-thirds of the postero-external column of the left side.

A few degenerated fibres are also seen in lumbar 2 in a like position, but below this level the cord is normal.

Case 5.—William C., aged 5. Out-patient at the London Hospital, September 4, 1897. Died September 18, 1897.

SUMMARY.

The child came to the hospital with the eruption out over the area of the 11*th dorsal segment.*

Fourteen days afterwards he died of exhaustion and slight broncho-pneumonia aided by starvation.

On microscopical examination, the 11*th dorsal ganglion was found to be infiltrated with small round cells, and two small hæmorrhagic foci were present. The remaining ganglia were normal.*

There was marked degeneration in the fibres of the 11*th dorsal posterior root on the left side. A few degenerated fibres were seen in the* 12*th dorsal root. The remaining roots were normal.*

Marked degeneration was seen to enter the cord with the 11*th dorsal posterior root of the left side. This degeneration could be traced up as high as the level of entry of the* 7*th dorsal root, but was then lost.*

Degeneration was found in the nerve-fibres on the peripheral side of the ganglion, both just after the posterior primary division has been given off and also a few inches from the patch on the skin.

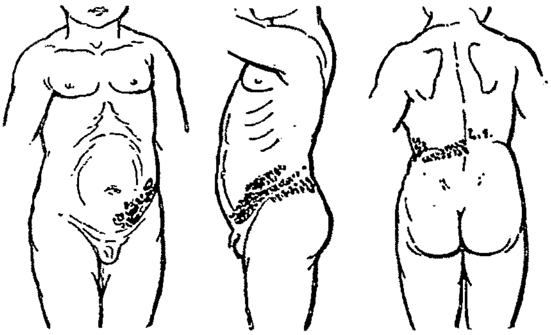

FIG. 5.

To show the distribution of the eruption in Case 5.

The patient came to the receiving room at the London Hospital on September 4, complaining of pain in the abdomen. A few spots of herpes were visible. On September 9 he was again seen, and the herpes was fully developed over the area in fig. 5. The child did not seem ill, but he "lay about." His temperature was 99·6° F. (37·6° C.). No cough. No physical signs in the chest. Nothing could be felt in the abdomen. Bowels opened. Marked swelling of glands in left groin.

On September 18, fourteen days after the eruption, the parents came to say that the child had died in the afternoon. One of us made a *post-mortem* examination with the following result:—

POST-MORTEM EXAMINATION.

Forty-eight hours after death, in cool weather.

The body was much emaciated and there were still unhealed and scabbed sores over the territory recently occupied by the eruption.

Heart normal.

Lungs normal, except for a little bronchitis and a very few scattered patches of broncho-pneumonia at both bases.

The stomach and small intestine were empty.

Liver, spleen, and kidneys normal.

The brain was normal. Vessels normal.

It is probable that owing to the extreme poverty of the parents the child died of collapse induced by starvation. There was no food in the house, and several of the other children were evidently suffering from hunger. The mother stated that she had had no food in the house for two days, and every particle of furniture had been sold.

MICROSCOPICAL EXAMINATION.

An examination was made of (*a*) a series of posterior root ganglia; (*b*) a series of spinal nerve-roots; (*c*) certain peripheral nerves; (*d*) the spinal cord.

(*a*) *Posterior Root Ganglia.*

An examination was made of the 9th, 10th, 11th, 12th dorsal, and 1st lumbar ganglia of both sides. The ganglia were hardened in 96 per cent. alcohol and embedded in paraffin in such a way that the ganglion of the right and of the left side at each level was contained in the same block. Each block containing two ganglia was cut and stained in strict series. The sections were stained by Nissl's method and counterstained with saffranin or with erythrosin.

Dorsal 11. *Left.*—In transverse serial sections of this ganglion, beginning at the exit of the posterior root, no change is seen at first, except an increase in the small round deeply-staining cells of the interstitial tissue. But as soon as the fibres of the posterior root begin to spread out in the substance of the ganglion, these small round cells increase in number (plate 3, figs. 1 and 2). At one point on the periphery of the ganglion they form an inflammatory focus, in the centre of which a small hæmorrhage is visible. Further along the series, at about the centre of the ganglion, this hæmorrhage increases in size and appears as a straw-coloured mass in the centre of a compact focus of deeply-staining small round cells. This focus extends throughout the ganglion until that part is reached where the peripheral sensory nerve trunk begins to be distinctly formed. Thus, throughout fifty sections passing through the centre of the ganglion a distinct hæmorrhage is visible situated on the periphery of the ganglion just below its sheath, and this hæmorrhage is surrounded by small round cells. Within this area the ganglion cells stain a uniform blue and appear as dark blue undifferentiated masses. Here and there, however, especially close to the borders of the straw-coloured hæmorrhagic mass, the colourless remains, or "ghosts," of ganglion cells are seen. Even the nucleoli of such cells are only very faintly stained. In addition to this definite focus, small round cells are seen to be in excess throughout this ganglion.

Dorsal 11. *Right.*—No abnormality of any kind in the ganglion cells or interstitial tissue is present in this ganglion.

Dorsal 9, 10, *and* 12, *and Lumbar* 1. *Right and left.*—All normal.

(*b*) *Posterior Nerve-roots.*

The 10th, 11th, and 12th dorsal nerve-roots were stained by Marchi's method, cut transversely and longitudinally, and also carefully teased.

Dorsal 10. *Right and left.*—Normal.

Dorsal 11. *Left.*—Many fibres in this root show undoubted degeneration of the acute type. These fibres are seen in longitudinal section scattered over the field, and are not collected into a bundle.

Dorsal 11. *Right.*—No degeneration.

Dorsal 12. *Left.*—In this root there seem to be a few definitely degenerated fibres. The black dots are jet black, lie in rows, and with a high power can be seen to lie definitely in the substance of the nerve-fibre. There are also a considerable number of leucocytes which stain black, possibly owing to their having picked up products of degeneration.

Dorsal 12. *Right.*—Normal. The longitudinal sections are very clean Marchi's specimens, and show no change resembling that seen in the left nerve-root.

(*c*) *Peripheral Nerves.*

The peripheral nerves connected with the 10th, 11th, and 12th dorsal ganglia were stained by Marchi's method and cut transversely and longitudinally and also teased.

Dorsal 10. *Right and Left.*—Normal.

Dorsal 11. *Left.*—Shortly before the nerve enters the ganglion it is seen to contain a small number of definitely degenerated fibres.

Nearer the periphery, at a short distance from the herpetic patch on the skin, a few distinctly degenerated fibres are seen.

Dorsal 11. *Right.*—No change.

Dorsal 12.—No degeneration in the nerves of either the right or left side.

(*d*) *The Spinal Cord.*

The cord was stained by Marchi's method after hardening in Müller's fluid, and sections were cut of every segment from the 3rd cervical to the 3rd lumbar (plate 11, fig. 1).

Beginning from below upwards, no change is seen until the level of entry of the 11th dorsal root is reached. Here there is obvious and extremely marked degeneration of the fibres that enter from the posterior root on the left side. At the level of entry of the 10th dorsal root the degeneration is seen to the inner side of the posterior horn, but the entering root is free from blackened fibres. At the level of the 7th dorsal root degenerated fibres can still be seen in the postero-external column, but all degeneration disappears at the level of the entry of the 6th dorsal root. The cord above this point is normal.

Thus the degeneration can be traced upwards in the spinal cord for three segments only above the entry of the affected root.

Case 6.—Robert M., aged 35, clerk. Admitted to Rainhill Asylum August 21, 1896. Died February 9, 1897.

SUMMARY.

Admitted to Rainhill Asylum August 21, 1896, *suffering from dementia paralytica.*

December 14, 1896, *he developed herpes zoster over the area in fig.* 6, *corresponding to the 3rd cervical.*

He died from seizures of dementia paralytica on February 9, 1897, *fifty-seven days after the appearance of the eruption.*

On microscopical examination the following changes were found:—

(*a*) *Posterior root ganglia.—The 3rd cervical ganglion of the left side was severely diseased. A considerable segment was entirely denuded of nerve-cells and nerve-fibres, and the ganglionic sheath investing the affected area was thickened.*

(*b*) *Posterior spinal roots.—The 3rd cervical root of the left side showed marked sclerosis and signs of an acute degeneration, the products of which were being absorbed. Some bundles of the 4th*

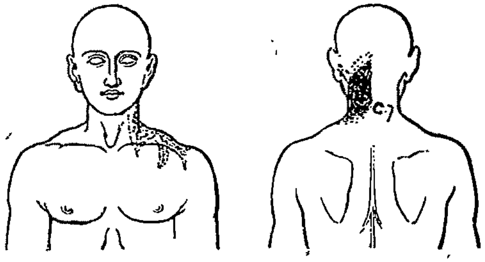

FIG. 6.

To show the distribution of the eruption in Case 6.

root on the left side also seemed to have undergone change, but this was a less certain change than that of the 3rd root.

(*c*) *Peripheral nerves.—The trunk and branches of the 3rd, and to a less extent of the 4th cervical nerve, were partially sclerosed, the change being more marked at the periphery than in the neighbourhood of the ganglion.*

(*d*) *Spinal cord and medulla oblongata.—The entering fibres of the 3rd cervical posterior root on the left side were markedly degenerated, and a few degenerated fibres seemed to enter the cord at the level of the 4th and possibly the 2nd cervical root on the left side. These fibres collected in a systematised field of degeneration which could be traced up to the nucleus cuneatus of the same side.*

Clinical.— No history obtainable. On admission he was extremely demented. The pupils were contracted (3 mm.) immobile and the margins uneven. Deep and superficial reflexes much exaggerated. Muscles in general wasted and paretic; locomotion impossible. Tongue could not be protruded and was very tremulous. Articulatory trouble so marked that he could not even pronounce his own name. Pulse 86, regular. Heart, lungs, genito-urinary and alimentary systems normal.

December 14, 1896. Developed severe herpes on the back of the neck on the left side over the area indicated in fig. 6. The vesicles soon became confluent, and the hair covering the portion of scalp affected was matted together by exudation. The eruption was accompanied by no rise of temperature or alteration in his general physical or mental condition.

December 28. The skin of the margin of the eruption was beginning to look healthy, but at the centre there was still marked scabbing and reddening; the hair of the affected scalp was falling out.

On January 17, 1897, he had three seizures, and it was noted that he had fallen off greatly in weight.

On January 27 he had five more seizures, on February 2 another, on February 9 three more, and from the last of these he did not rally.

Interval between the date of the herpetic eruption and the date of death, fifty-seven days.

Post-mortem Examination.

The examination was made thirteen hours after death in cold weather. Body thin, almost emaciated; skeletal and muscular development poor; no localised muscular atrophy, and no contractures.

In the portion where the herpetic eruption had been most intense, the skin was white and smooth, and there were some scabs; there was also a bald patch of occipital scalp along the lower border on the left side.

Calvaria of average size, slightly thickened and increased in density; dural sinuses partly filled with *post-mortem* blood clot; dura mater slack anteriorly, no localised thickening or unusual adhesions to bone or arachnoid. A marked excess of clear watery cerebro-spinal fluid. The encephalon weighed 1,135 grammes.

The main cerebral vessels showed general thickening, but there was no calcification.

The arachnoid presented the universal opacity and thickening characteristic of advanced general paralysis. The pia mater was markedly thickened and slightly anæmic. It was very adherent, and decortication attended its removal; this was most pronounced over the central convolutions.

The brain was a small one, but the hemispheres were equal and the segments proportionately developed. The convolutions were rather complexly arranged, but were generally wasted, the atrophy being most noticeable frontally. The sulci were all wide and shallow.

The right hemisphere, with its membranes, weighed 487 grammes, the left 497 grammes.

The cortex cerebri was dark in colour, firm, slightly anæmic, reduced in depth and indistinctly striated.

The white substance was of healthy colour and consistence, and normal vascularity. The lateral ventricles were enlarged, and contained an excess of fluid, and the ependyma was slightly granular.

The basal nuclei were free from focal lesion.

The corpus callosum and other commissures were healthy.

The cerebellum weighed 137 grammes, its cortex was dark and thin, and its general consistence firm.

In the pons there was no noteworthy change.

The gray and white tissues of the medulla oblongata were healthy to the naked eye, but the ependyma of the fourth ventricle was very thick and granular.

The pons and medulla together weighed 30 grammes.

The cranial nerves were healthy to the naked eye.

Adhesions of an abnormal character existed between the dura and arachnoid all along the dorsal aspect of the spinal cord; the pia-arachnoid was unusually opaque, and there was an excess of cerebrospinal fluid.

The spinal nerve-roots and posterior root ganglia in the cervical region of either side presented no gross macroscopic change.

The superior and middle cervical sympathetic ganglia also appeared the same on both sides to the naked eye.

Nine ribs on the right side and seven on the left showed old fractures. Those on the right side were the 2nd, 3rd, 4th, 5th, 6th, 7th, 8th, 9th, and 10th; and of these the 5th, 6th, 7th, 9th, and 10th were fractured in two places. All these ribs were broken at points between one and two inches from the costochondral articulation, and in the case of those which were broken twice, the second fracture was situated some three inches or more from that joint. The broken ribs on the left side were the 4th, 5th, 6th, 7th, 8th, 9th and 10th; several of these were fractured in two places, and the break in every case lay between one and three inches from the costo-chondral joint. All these fractures were of old-standing, and in the case of the majority firm union had occurred, but in some (more particularly the lower ones) slight movement could be obtained at the site of the fracture. There was considerable displacement in some instances, and around all much callus had been thrown out. They were probably all of the same age (about six months). The right pleural cavity was obliterated by old fibrous adhesions; the left was free.

The general colour of the lungs was dark and a few broncho-pneumonic patches were found in both.

The pericardium contained a normal amount of clear fluid.

The heart was of rather small size and weighed 8 oz. (226 grammes), its muscle was dark and firm. Little clot was present in its chambers, there was no organic disease of valves or aorta.

Peritoneum healthy.

The liver weighed 39 ozs. (1,103 grammes). Some old adhesions existed between the upper surface of the right lobe and the diaphragm. Its substance was dark and firm on section and the gall bladder was healthy.

Spleen dark and firm; weight 3 ozs. (84 grammes).

The capsules of the kidneys stripped cleanly, the substance was dark and firm, and the organs were small. The right kidney weighed 3 ozs. (84 grammes), the left 3½ ozs. (99 grammes).

The suprarenal glands, stomach, pancreas, intestines and bladder were normal.

On the foreskin of the penis the existence of some scars pointed to previous syphilitic infection, and there was excess of fibrous tissue in both testicles.

MICROSCOPIC EXAMINATION.

A microscopic examination was made of (*a*) a series of posterior root ganglia, (*b*) a series of spinal nerve-roots, (*c*) a series of peripheral spinal nerves, (*d*) the superior cervical sympathetic ganglia, (*e*) the spinal cord and medulla oblongata.

(*a*) *Posterior Root Ganglia.*

The posterior root ganglia examined were the 2nd, 3rd, 4th, 5th and 6th cervical of both sides.

Cervical 3. *Left.*—The ganglion was hardened in formalin 4 per cent., and without further preparation fixed in gum on a freezing microtome, and cut transversely but not serially. Numerous sections were stained (*a*) for the display of nerve-cells by the method of Nissl, (*b*) for the display of connective tissues with Mallory's hæmatoxylin, (*c*) for the display of nerve-fibres by an original method with osmic acid and hæmatoxylin, which may be briefly described as follows :—

(1) Warm for a few minutes in osmic acid 1 per cent. until sections brown.

(2) Wash thoroughly in water.

(3) Warm for a few minutes in the solution of hæmatoxylin employed in the Weigert-Pal method.

(4) Wash in water and decolorise by method of Pal.

(5) Counterstain with Held's solution of erythrosin.

The majority of the sections, however stained, show important alterations (plate 5).

On that side of the ganglion furthest away from the anterior root is an extensive diseased field of crescent shape, the convexity of the crescent being represented by the circumferential margin of the ganglion, round about two-thirds of which it stretches. This focus extends inwards for about 1·275 mm., so as to invade from a quarter to one-third of the sectional field of the ganglion. The affected substance is composed of small round cells arranged in masses and in lines, of fields of coarse fibrous tissue and of newly-formed blood-vessels, and it is remarkable that every single nerve-cell and nerve-fibre has disappeared from this area. The line of demarcation between the healthy and diseased fields, under a low power of the microscope, looks abrupt and definite, but under a higher power one can make out that some of the nerve-cells on the border line are degenerated.

The remainder of the substance of the ganglion is healthy. But that part of the sheath of the ganglion which covers the affected area is greatly thickened, its component lamellæ are widely separated from one another, infiltrated by numbers of small round cells, and rich in thickened and congested blood-vessels. The anterior root as it passes round the ganglion is normal.

It is unfortunate that this ganglion was not cut in series so that the seat of maximum affection might be correctly localised, but as the sections toward either end of the ganglion are less affected than the central ones it appears that the diseased focus is situated mainly in the median longitude of the body.

Cervical 3. *Right.*—Stained and cut in the same way as the ganglion just described. It shows no change and differs fundamentally from the corresponding ganglion of the opposite side.

Cervical 2, 4, 5 *and* 6. *Right and left.*—Show no change.

(*b*) *Spinal Nerve-roots.*

Both anterior and posterior roots were stained by Marchi's method, and cut longitudinally and transversely.

Cervical 3. *Left.*—Where the roots pierce the dura, three bundles of the sensory root are undergoing acute degeneration, or have undergone degeneration, and the products are already partly absorbed. For these bundles have a hazy look, their component fibres are blurred and swollen, and the fat droplets are gray in colour. In the neighbourhood of these three bundles are others which are to some extent sclerosed.

In sections nearer to the ganglion where the sensory and motor roots can be more readily differentiated, about one-third of the fibres of the sensory root have disappeared, and are replaced by fibrous tissue. These diseased bundles are clumped together at one end of the section (plate 16, fig. 2).

The anterior root is perfectly healthy and shows none of these changes.

Cervical 3. *Right.*—This root shows no change.

Cervical 4. *Left.*– There is slight apparent thickening of the sheath over one bundle, but this may be due to the obliquity of the section. If there is any change it is extremely slight.

Cervical 4. *Right.*—Normal.

Cervical 2, 5 and 6. *Right and left.*—Show no change.

(c) *Conjoint Peripheral Nerves.*

Stained by Marchi's method, and cut transversely and longitudinally.

Cervical 3. *Left.*—This nerve presents a very striking appearance. In the more peripheral sections when the nerve is split up into numbers of small bundles there is hardly one that is not markedly sclerosed. In sections nearer the ganglion where the bundles are large the sclerosis is less evident.

Cervical 3. *Right.*—This nerve shows no change.

Cervical 4. *Left.*—The sensory bundles close up to the ganglion show scattered sclerosis. Towards the periphery three bundles appear to be absolutely sclerosed.

Cervical 4. *Right.*—No change.

Cervical 2, 5 *and* 6. *Right and left.*—Normal.

Great occipital nerve. Left.—Stained by Marchi's method. No individual bundle possesses quite its full complement of fibres, and in three bundles in particular there is a great falling out of nerve-fibres and a replacement by fibro-cellular tissue. There is practically no acute degeneration, and the perineurium looks healthy. The blood-vessels have thickened walls.

Great occipital nerve. Right.—There is absolutely no acute degeneration. No patches of sclerosis are seen as on left side.

Small occipital nerve. Right and left.—No obvious degenerative alteration.

(d) *Superior Cervical Sympathetic Ganglia.*

Right and left.—These ganglia were hardened in formalin 4 per cent., and sections were stained—(1) by the method of Nissl, (2) with Mallory's hæmatoxylin, (3) with osmic acid and hæmatoxylin, as those of the 3rd cervical posterior root ganglia. This method displays the non-medullated fibres well, but by none of the processes were morbid changes discovered.

(e) *Spinal Cord and Medulla Oblongata.*

Stained by the method of Marchi (plate 10, fig. 2).

Cervical 3.—Both transverse and longitudinal sections were cut at the level of entry of the 3rd cervical roots.

The extraspinal portion of the left posterior root as it appears in these sections is almost entirely free from acute degeneration, but is sclerosed. No acute degeneration can be seen in Lissauer's root zone. But immediately after entering the cord the posterior root-fibres show typical acute degeneration which can be clearly made out in both longitudinal and transverse sections. There is further, a field of acutely degenerated fibres in the left postero-external column, which on transverse section is seen to hug the posterior cornu. These diseased fibres are most numerous opposite the substantia gelatinosa Rolandi, whence the field tapers inwards and ends about two-thirds of the way along the posterior horn.

In the centre of the gray substance of the left posterior cornu is another isolated small collection of degenerated fibres.

Cervical 2.—*Transverse and longitudinal sections.*—In the outer part of the left postero-external column the above-mentioned strip of degeneration is very clearly seen. It is again widest in its most dorsally situated part, and tapers inwards as before, but it is not now so closely applied to the margin of the cornu.

Fibres of large and small size are commingled in the degenerated area. In the intraspinal but not in the extraspinal portion of the entering left posterior root are a few acutely degenerated fibres. Indications of degeneration are again visible in the gray substance of the left posterior cornu.

There are a few degenerated fibres in the lateral columns on both sides, such as are so commonly found in cases of dementia paralytica.

The pia-arachnoid is perhaps a little thick and more cellular than normal, but there is no localised meningitis. The arteries in places show signs of arteritis.

Cervical 1.—In the lateral one-third or one-fourth of the left funiculus cuneatus is a prominent field of degenerated fibres, extending from the nucleus cuneatus, which is here forming, to the periphery. These fibres are more numerous in the ventral than in the dorsal portion. On a rough estimate there are about 500 diseased fibres, and they are mainly of small calibre.

Medulla Oblongata.—Immediately above the pyramidal decussation there is a well-marked collection of degenerated fibres in the outer one-third of the left funiculus cuneatus, and this is continuous with a thin line of diseased fibres, which skirts the periphery of that column. A few degenerated fibres are also visible in the cuneate nucleus.

Medulla oblongata. Level of lower end of great olive.—The degenerated fibres lie in that part of the funiculus cuneatus which is nearest to the sensory root of the fifth nerve and the substantia gelatinosa Rolandi. Their number has diminished greatly

Medulla oblongata. At lower end of fourth ventricle.—The degenerated fibres can still be traced in the lateral portion of the funiculus cuneatus, and some diseased fibres are seen streaming into the so-called external cuneate nucleus which is appearing at this level. A band of external arciform fibres lies between the degeneration and the surface; these fibres and likewise the internal arciform fibres are free from degeneration.

Medulla oblongata. Through middle of great olive.—Round the left nucleus cuneatus on its dorso-lateral and ventral aspects are a few scattered degenerated fibres. A few black dots are also present within the nucleus.

It is impossible, owing to the method of staining, to say anything definite concerning changes in the nerve-cells of the nucleus.

Medulla oblongata. Through upper end of nucleus cuneatus.—At the periphery fringing the left nucleus cuneatus just a few degenerated fibres can be defined, and there are also a few black dots in the substance of the nucleus.

Higher than this the degeneration is not traceable.

Spinal Cord below the entry of the affected Root.

Cervical 4.—There are just a few scattered degenerated fibres of small calibre in the dorsal and lateral part of Burdach's column on the left side, and a very few degenerated posterior root-fibres seem to be entering at this level.

Cervical 5.—A very few black dots are seen along the inner margin of the left posterior cornu. These may be descending collaterals, but it is difficult, owing to their small number and scattered appearance, to be sure if they can bear this interpretation.

Cervical 6.—No change in posterior columns.

Cervical 7, 8 *and Dorsal* 1.—No change in the posterior columns.

All the sections of medulla oblongata and spinal cord show disseminated degenerated fibres in both pyramidal tracts associated with the dementia paralytica from which this patient suffered.

Case 7.—Frank C., aged 32. Admitted to Guy's Hospital (Dr. Hale White), April, 1895. Died September 2, 1895.

SUMMARY.

A man of 32 *suffered for a year with progressive anæmia and enlargement of the spleen, for which he took arsenic over a considerable period. On admission to Guy's Hospital both spleen and* *liver were found to be enlarged, and there was some enlargement of the lymphatic glands. The blood showed marked increase of polynuclear leucocytes with eosin-staining granules.*

On May 29, 1895, he developed a profound eruption of herpes zoster over the area in fig. 7 corresponding to the 2nd dorsal.

His general condition became gradually worse, and he died on September 2, 1895, ninety-six days after the eruption first began to appear.

Post-mortem examination showed marked general enlargement of the spleen. The liver was also enlarged and contained collections of leucocytes throughout its substance. The marrow of the long bones was replaced by a yellow jelly-like mass.

The site of the previous herpetic eruption was extremely clearly marked out by brown pigmented patches.

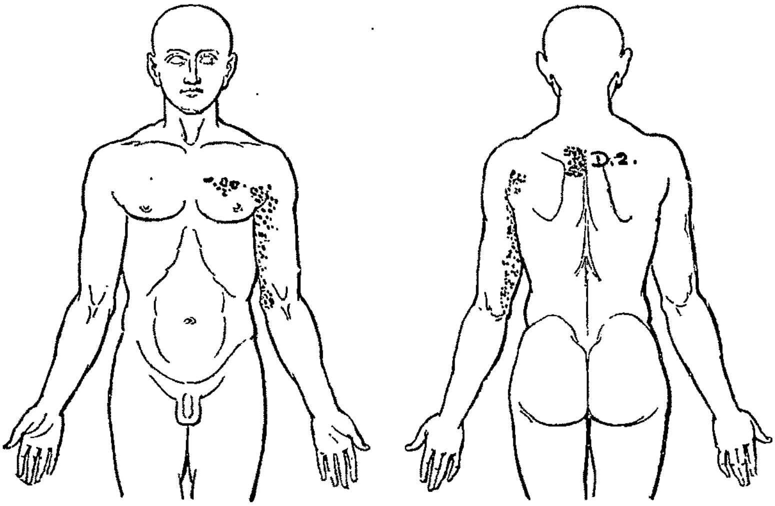

FIG. 7.

To show the distribution of the eruption in Case 7.

On microscopical examination the following changes were found :—

(a) Posterior root ganglia.—The 2nd dorsal ganglion of the left side showed a distinct local lesion destroying the nerve-cells and fibres over a considerable extent of the body.

(b) Posterior spinal nerve-roots.—In the 2nd dorsal posterior root of the left side several nerve fasciculi were manifestly diseased; with the method of Marchi these bundles presented on the whole a pale sclerosed aspect, but they also contained the partially-absorbed remnants of an acute degenerative process.

In the 3rd dorsal root of the same side a few degenerated fibres could be recognised.

(*c*) *Peripheral nerves.—Some bundles of the left 2nd dorsal conjoint trunk were altered similarly to the 2nd dorsal posterior root. There were no obvious changes in the 3rd dorsal nerve.*

(*d*) *Spinal cord.—Many nerve-fibres which entered from the 2nd dorsal posterior root of the left side and a few fibres from the 1st dorsal root were acutely degenerated, and these fibres collected to form a systemic field of degeneration which could be followed up as far as the left nucleus cuneatus.*

History.—In April, 1894, he began to suffer from attacks of pain in the left side with cold sweats at night. In June his abdomen and feet began to swell. In November the extraction of two teeth was followed by profuse bleeding lasting forty-six hours.

He served in the army, but for the last three years has been a general labourer.

He took arsenic from August, 1894, to March, 1895, in the Croydon Hospital.

There is no history of syphilis.

On admission, he was somewhat wasted. The anæmia was not very marked.

The abdomen was distended, and on palpation a splenic tumour could be felt occupying the left hypochondriac and lumbar regions. Its surface was smooth and its edge even. The tumour edge began at the ensiform cartilage and extended downwards to a point 1½ inches (3·75 cm.) to the right of the umbilicus and reached below to within 1 inch (2·5 cm.) of the iliac crest.

The liver was enlarged, and the edge could be felt below the costal margin. Some ascites was present.

The inguinal, axillary, and right posterior cervical glands were enlarged.

Heart normal, except that a systolic bruit was heard at the apex. Examination of the blood showed that the white corpuscles were much increased. The majority of the white corpuscles were larger than usual, containing two or three neucleoli, and with granules that stained with eosin.

Urine was normal.

Progress of the case.—Spleen varied in size but did not greatly increase. Temperature was raised each night.

May 29. Herpes zoster appeared over the area in fig. 7. The vesicles appeared on an inflamed base, enlarged, and became confluent, forming bullæ. Extremely marked pain was present which continued on and off until August. The vesicles healed, but the whole area on which the eruption had appeared was covered by dark brown pigmented scars, probably due to the fact that he had been taking arsenic until within a fortnight of the eruption.

The patient became extremely thin, and he began to have attacks of diarrhœa. The temperature was permanently raised, with nightly exacerbations. He became gradually weaker, and died on September 2, 1895, ninety-six days after the appearance of the eruption.

Post-mortem Examination.

Made twenty-four hours after death. The position of the herpetic eruption was extremely well marked out by dark stains on the skin.

Both pleural cavities contained fluid. The upper part of both lungs was emphysematous and œdematous.

Spleen weighed 84 oz. (2·37 kgm.), and was soft and smooth. It contained a large infarct.

Liver weighed 85 oz. (2·4 kgm.). Throughout its substance were collections of leucocytes.

Heart normal.

The femur contained a jelly-like yellow mass replacing the absorbed cancellous tissue. The marrow of the sternum was very pale.

The nervous system showed no naked-eye change, and was preserved for microscopic examination.

Microscopical Examination.

A microscopic examination was made of:—(*a*) a series of posterior spinal root ganglia, (*b*) a series of spinal nerve-roots, (*c*) a series of peripheral nerves, (*d*) the spinal cord.

(*a*) *Posterior Root Ganglia.*

The following ganglia were examined:—The 2nd, 3rd, 4th, 6th, 7th and 8th cervical, and the 1st, 2nd, 3rd, 4th and 5th dorsal, all of the left side.

The method of examination employed in the case of each ganglion was as follows:—The entire ganglion along with the attached spinal nerve-roots and a portion of the conjoint peripheral nerve-trunk was stained *en bloc* by the method of Marchi. After imbedding in celloidin, serial sections were made in the longitudinal direction, and every alternate section of the series was mounted.

Dorsal 2.—Of the twenty-three sections mounted the first six show remarkable changes in the sheath and body of the ganglion (plate 7). The sheath is thickened and blurred all round, it is infiltrated by small round cells, and its contained blood-vessels are extremely congested with red blood corpuscles. Within the sheath in the substance of the ganglion there is not a single nerve-cell or nerve-fibre of any kind to be made out, the place which they should occupy being entirely filled up by a collection of foreign tissue which does not stain with osmic acid, and in which lie numerous collections of brown coarsely-granular amorphous pigment and many congested blood-capillaries.

In the next two or three sections the ganglionic field exhibits a transition stage between a healthy and a diseased condition, that is to say, some portions of the field are occupied by morbid tissue as above described, others by normally arranged collections of nerve-fibres and nerve-cells. With regard to the structure of these nerve-cells nothing definite can be stated, as the method of Marchi is not adapted for displaying them, but of the bundles of nerve-fibres a considerable number are acutely degenerated, with rows of irregular-shaped black masses running along the course of these fibres; other bundles seem to be to a large extent sclerosed.

In the remaining sections the ganglion, so far as can be judged from the method of Marchi, presents a healthy appearance, nerve-cells and nerve-fibres are abundant, and there is a complete absence of any destructive change.

Thus over a certain area of the ganglion the sheath is thickened and diseased, and the ganglionic substance subjacent to this portion of altered sheath is destroyed to about one-fourth of the depth of the whole ganglion.

Dorsal 1.—The blood-vessels in the connective tissue in the environment of the ganglion show marked congestion, but this is a common appearance not to be regarded as pathological. The nerve-cells and nerve-fibres seem to be normally represented, and with the exception of one or two minute pale-stained granular foci of doubtful significance no change is manifest.

Cervical 8, 7, 6, 4, 3 *and* 2.—The ganglia show no noteworthy change.

Dorsal 3, 4 *and* 5.—The ganglia show no noteworthy change.

(*b*) *Spinal Nerve-roots, Anterior and Posterior.*

Dorsal 2.—The major portion of the posterior root appears to be healthy, or only shows an acutely degenerated fibre here and there, but there are several bundles which exhibit changes of a pronounced character. Most noticeable is a deficiency in number of healthy fibres and a substitution for them of unstained fibro-cellular tissue; in short, a form of sclerosis. Scattered over the same field are rows of irregular-shaped blackened fatty particles, indicating nerve-fibres actually undergoing disintegration, and in the same field an abnormal number of congested capillaries are distinguishable.

A continuity between these diseased bundles and the focal lesion described under the heading of the second dorsal ganglion can be traced.

The anterior root is not degenerated.

Dorsal 1.—Some few nerve-fibres in the posterior root seem to be undergoing degeneration, but the change is by no means a striking one.

The anterior root is normal.

Cervical 8, 7, 6, 4, 3 *and* 2.—All normal.

Dorsal 3, 4 *and* 5.—All normal.

(*c*) *Conjoint Peripheral Nerve-trunks.*

Dorsal 2.—Examined near the ganglion. The major portion of the conjoint trunk seems to be healthy, but there are one or two bundles which are in large measure sclerosed, and also contain a few acutely degenerated fibres and many congested capillaries. There are likewise degenerated fibres in considerable numbers in what seems to be the posterior primary division of the nerve.

Dorsal 1.—There are a few fibres visible which seem to be degenerated, but the evidence of degeneration is not pronounced.

Cervical 8, 7, 6, 4, 3 *and* 2.—All normal.

Dorsal 3, 4 *and* 5.—All normal.

(*d*) *Spinal Cord.*

Method of examination.—Portions of the cord were taken from the levels of entry of all nerve-roots from the 1st sacral to the 1st cervical inclusive. These blocks were stained by the method of Marchi and cut transversely and in some cases longitudinally as well (plate 10, fig. 1).

Dorsal 2.—In transverse section degenerated fibres are seen to enter in the left posterior root, and a well-defined strip of diseased fibres is seen hugging the inner margin of the left posterior cornu. This field of degeneration extends from the periphery to a point about midway along the cornu, it tapers off internally, is thickest at about its middle, and, in that part of it situated next the periphery, the degenerated entering root-fibres are cut longitudinally or obliquely.

This can hardly be called a " mass degeneration," because the individual diseased fibres are all separated from one another by interposed healthy tubules, and on a rough count their total number only just exceeds 300.

It is to be further noted that in the centre of the gray substance of the left posterior horn, immediately ventral to the substantia gelatinosa, a few diseased fibres of small calibre are seen cut transversely.

The postero-external column of the right side is normal, and all other columns are also free from degeneration. Special attention must be drawn to the fact that all the degeneration in the spinal cord is essentially of an acute nature, and that there is no indication whatever of post-degenerative sclerosis in any part of the intraspinal course of the degenerated posterior root-fibres.

This is an important fact, because, as has already been mentioned, examination of the affected posterior root prior to its entry reveals the predominance of a sclerotic over an acute degenerative change.

Dorsal 1.—Transverse sections opposite the level of entry of the posterior roots show that the field of degeneration in the left postero-external column noted in dorsal 2 is translated slightly inwards, so that while the inner tapering portion still hugs the posterior cornu, the more dorsal thicker portion is separated from the cornu by an appreciable interval. Again, a few acutely degenerated fibres are seen entering in the left posterior root, and there also appears to be a slight increase in the numerical strength of the fibres in the degenerated field. Again, also, a few degenerated blackened fibres are visible in the gray substance of the posterior cornu just ventral to the gelatinous substance.

Longitudinal sections at this level well display the degenerated fibres which have entered at dorsal 2, and likewise confirm the point above mentioned, that a few diseased fibres are entering from the 1st dorsal root of the left side.

Cervical 8.—The degenerated fibres are scattered in comma form in the left postero-external column. The head of the comma is at the periphery, the tail touches the posterior horn at a point rather more than half way down its inner margin, and the convexity is directed towards the middle line. A space is thus left between the area of degeneration and the dorsal half of the posterior cornu, which contains practically no degenerated fibres.

Cervical 7.—The field of degeneration maintains its comma form but is placed still further inwards; the head of the comma lies in the inner half of the postero-external column at the periphery, its convexity touches the intercolumnar septum, and the tail gradually tapering off just reaches the inner margin of the neck of the posterior cornu not far behind the posterior commissure.

Cervical 6.—The field containing degenerated fibres is becoming cuneiform. It is situated mainly in the inner and posterior angle of the postero-external column. The tail of the above-mentioned comma is disappearing and degenerated fibres no longer touch the posterior horn.

Cervical 5.—The degenerated fibres are clumped together in a wedge-shaped area at the posterior and inner angle of the postero-external column.

Owing to a gradual disappearance of degenerated fibres which has been occurring all the way up the cervical region, the total number of diseased fibres at this level is considerably diminished when compared with the sections at the level of dorsal 1.

Cervical 4.—The degenerated fibres lie in a similar position to that they occupied at cervical 5, but the field has lost its wedge shape, and is beginning to retreat from the periphery.

Cervical 3.—The degeneration is still further removed from the periphery.

Cervical 2.—The degenerated fibres are very sparsely scattered at this level, and indeed difficult to locate at all, but a careful examination leaves no doubt of the existence of a few, and these from their position are evidently making for the head of the nucleus of the left funiculus cuneatus.

Cervical 1.—Similar to cervical 2.

In sections higher up, showing the cuneate nuclei, it can just be made out that degenerated fibres enter the inner side of that body.

Case 8.—Elizabeth B., aged 76. Admitted to Marylebone Infirmary (Mr. Lunn), January, 1895. Died February 18, 1896.

SUMMARY.

Admitted with right hemiplegia and in a demented condition. November, 1895, *had another "fit."*

November 7, 1895, *developed an acute attack of zoster over the area in fig.* 8.

She died from pneumonia on February 18, 1896, 103 *days after the attack of zoster.*

On post-mortem examination the left cortex showed two areas within which the whole cerebral substance had been destroyed. The outer surface of the right hemisphere of the cerebellum showed a similar area of softening.

On microscopical examination the following changes were found:—

(a) Posterior root ganglia.—The 12*th dorsal ganglion of the right side showed a pronounced focal lesion destroying nerve-cells and nerve-fibres over a considerable extent of the body.*

(b) Posterior spinal nerve-roots.—In the 12*th dorsal root of the right side a number of fasciculi exhibited manifest changes. Nerve tubules had disappeared and were replaced by fibro-cellular elements and collections of partially-absorbed degenerative products.*

(c) Peripheral nerves.—The 12*th dorsal conjoint trunk of the right side was similarly affected to the above-mentioned posterior root.*

(d) Spinal cord.—As soon as the fibres of the 12*th dorsal posterior root of the right side entered the cord, they showed the typical staining reaction of acute degeneration, and pursuing the recognised course of a root lesion, they could be followed along in the posterior columns as far up as the* 7*th cervical segment.*

Degeneration was also seen in the right lateral pyramidal and in the left direct pyramidal tracts, and a few degenerated fibres in the left lateral pyramid, due to the cerebral softening and connected in no way with the herpetic lesion.

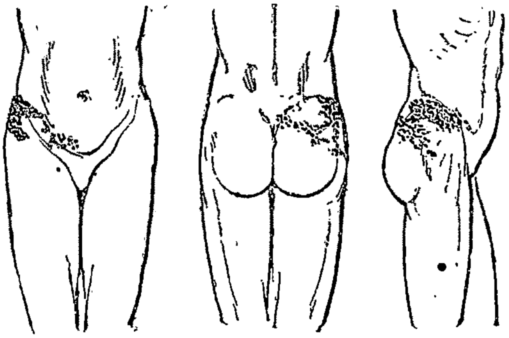

FIG. 8.

To show the distribution of the eruption in Case 8.

No history of her general condition could be obtained beyond the fact that she had long been an inmate of the Workhouse, and that she was admitted to the Infirmary in January, 1895, with right hemiplegia. She remained in a demented condition, passing urine and fæces under her, until November, 1895, when she had another "fit," in which the left half of the face and the left arm were convulsed.

On November 7, 1895, she developed an acute attack of herpes over the area in fig. 8.

At this time her condition was as follows:—She could not name any object at sight, but had no sign of motor aphasia. Right arm and right leg were absolutely paralysed, and both were in a condition of extreme contracture. Sensation to pain was everywhere present. The right knee-jerk could not be obtained, but this was possibly due to marked changes in the joint. Left knee-jerk was just obtained. Both plantar reflexes were brisk, the right more so than the left. The right ankle was ankylosed, and thus could not be examined for ankle clonus. No ptosis, ocular paralysis or nystagmus were present. Pupils reacted to light and accommodation. Some weakness of movement was visible about the lower part of the right half of the face. She could only protrude the tongue to a slight extent. Incontinence of urine and fæces.

All the arteries were extremely thickened and degenerated, but otherwise there was no noteworthy change in the circulatory or respiratory systems.

She died of pneumonia on February 18, 1896, 103 days after the attack of herpes zoster began.

POST-MORTEM EXAMINATION.

Made forty hours after death in bitterly cold weather. The post-mortem room was at the external temperature.

Rigor mortis well marked.

Well marked dark brown scaly scars were present over the area that had been occupied by the eruption.

No bedsores or other changes in the skin.

Some turbid yellow fluid was present in the left half of the chest, and the parietal pleura on the left side was covered with flakey yellow lymph. The upper lobe of the left lung was solid, and the lower lobe airless and collapsed. The right lung was universally adherent and showed signs of general bronchitis.

The heart was normal, except that its walls were soft and fatty. The aorta was somewhat atheromatous.

Peritoneum normal. Liver somewhat fatty. Capsule of the spleen much thickened. Kidneys were slightly granular. Bladder normal.

Nervous system.—The spinal cord was beautifully firm throughout, and showed no gross anatomical change. The brain weighed 1,105 grammes; when separated the right hemisphere weighed 509 grammes, (stripped 481 grammes), the left hemisphere 424 grammes (stripped 396 grammes), the cerebellum 95 grammes.

The vessels were exceedingly tough and degenerated.

The brain was much shrunken and wasted, and the dura mater lay in folds.

On the outer aspect of the left cerebral hemisphere were two isolated areas, where the cortex and subjacent white substance had been destroyed for a long time owing to thrombotic arterial occlusion; both were situated in the posterior segment of the hemisphere. The larger patch, measuring about 4 cm. in its maximum vertical by 5 cm. in its greatest horizontal diameter, extended transversely from the posterior end of the sylvian fissure in front to within 1 cm. of the posterior margin of the occipital lobe behind, and vertically from 1 cm. below the horizontal limb of the intraparietal sulcus above to the posterior extremity of the 2nd temporal sulcus below. The entire cortex and the subjacent white substance down even to the ependyma of the posterior horn of the lateral ventricle, was destroyed over practically the whole angular and posterior parietal gyri and over parts of the supramarginal, occipito-parietal and occipito-temporal annectant gyri.

The smaller patch, measuring about 3 cm. in the vertical direction by 1·5 cm. in the horizontal, had its centre at the upper end of the ascending limb of the intraparietal sulcus and involved adjacent parts of the supramarginal and superior parietal gyri. The ascending parietal convolution had escaped.

On the inner aspect of the same hemisphere was another narrow patch of old-standing softening, beginning in front at the anterior end of the calcarine fissure and running horizontally backwards along that fissure to the tip of the occipital lobe. This lesion had destroyed all the cortical and subjacent white substance between the collateral and calcarine fissures, and it had spread upwards, involving the lower and hinder part of the cuneus.

Cerebellum.—On the under surface of the right hemisphere of the cerebellum was another extensive area of old-standing softening, measuring 4 cm. in the antero-posterior by 5 cm. in the lateral direction; internally this area reached to within about 1·5 cm. of the middle line; posteriorly and externally it almost touched the margin of the hemisphere, and anteriorly it approached to within a couple of cm. of the margin. It represented a destruction, to a depth of from 1·5 to 2 cm., of the outer third or half of the inferior anterior lobe, of the major part of the inferior middle and inferior posterior lobes, and of that part of the superior posterior lobe which is seen on the ventral and posterior aspect of the hemisphere. The area destroyed corresponded to the distribution of the right posterior inferior cerebellar artery. The nucleus dentatus was intact.

MICROSCOPIC EXAMINATION.

A microscopic examination was made of:—(*a*) a series of posterior root ganglia; (*b*) a series of spinal nerve-roots; (*c*) a series of peripheral nerves; (*d*) the spinal cord.

(*a*) *Posterior Root Ganglia.*

Of the posterior root ganglia the following were examined—the 5th, 8th, 9th, 10th, 11th and 12th dorsal, and the 1st and 2nd lumbar of the right side and the 8th, 9th, 10th, 11th and 12th dorsal, and the 1st and 2nd lumbar of the left side.

The method of examination employed in the case of each of these ganglia, with the exception of the 10th and 11th dorsal of the right side, was as follows:—The entire ganglion, along with the attached spinal nerve-roots, and a portion of the conjoint peripheral nerve-trunk, was stained *en bloc* by the method of Marchi, with the object of demonstrating whether any acute degeneration of medullated nerve-fibres existed. After embedding in celloidin, serial sections were cut in the longitudinal direction, and every section of the series was mounted. In the case of the 10th and 11th dorsal ganglia of the right side the block was divided into two equal halves; one portion was then cut longitudinally, the other transversely.

Dorsal 12. *Right.*—This ganglion shows profound changes (plate 8, figs. 1 and 2). Situated immediately beneath the capsule, mainly in the distal half of the ganglion, is a definite circumscribed focus of disease which extends inwards for a distance of 1·25 mm., and involves, roughly speaking, from one-fourth to one-third of the ganglion. This area has a deep brown uniformly granular aspect, and contains neither nerve-cells nor nerve-fibres; its outline is wavy, and its shape necessarily varies in different sections. It is obviously the broken-down remains of a large hæmorrhage, around which secondary sclerotic changes have occurred.

The sheath of the ganglion overlying this focus is markedly thickened by what appears to be a small round-cell proliferation, and the blood-vessels ramifying therein are extremely congested and stand out prominently. A zone of ganglionic substance lying in contact with and bounding the diseased focus, is also disorganised; it stains palely, and in it there is an apparent proliferation of fibro-cellular connective tissue elements. The blood-vessels within this zone are congested, and nerve-fibres and nerve-cells have disappeared.

In other parts the sheath of the ganglion looks healthy, and the remainder of the ganglionic substance contains nerve-cells and nerve-fibres in normal abundance. The method of Marchi, of course, does not permit of any judgment concerning the existence of fine changes in these nerve-cells. But in the strands of nerve-fibres intertwining the ganglion cells, marked indications of degeneration can be demonstrated. For in the first place, compared with sections of normal ganglia, the fibres are in parts scanty, and it looks as if a considerable number had entirely vanished as a result of past degeneration; and, secondly, along the course of many of those which remain, globules and lumps of blackened fat, typifying acute parenchymatous degeneration, may be seen.

Dorsal. Left.—This ganglion is normal and shows none of the changes seen in the ganglion of the opposite side.

Dorsal 5, 8, 9, 10 *and* 11. *Right and left.*—Show no change.

Lumbar 1 *and* 2. *Right and left.*—Show no change.

(*b*) *Spinal Nerve-roots, Anterior and Posterior.*

Dorsal 12. *Right.*—The bundles forming the posterior nerve-root show two important changes. Firstly, in a number of fasciculi there is a pronounced disappearance of healthy nerve tubules and a substitution of fibro-cellular connective tissue elements. In some bundles hardly a single medullated nerve-fibre can be discerned. Secondly, many of the fibres which remain are undergoing acute degeneration, and others show partially absorbed degenerative products along their course. The anterior root contains its full complement of nerve-fibres and shows no change resembling that seen in the posterior root.

Dorsal 12. *Left.*—Both posterior and anterior roots show no change.

Dorsal 8, 9, 10 *and* 11. *Right and left.*—Show no change.

Lumbar 1 *and* 2. *Right and left.*—Show no change.

(*c*) *Conjoint Nerve-trunks Peripheral to Ganglia.*

Dorsal 12. *Right.*—Close up to the ganglion, where the motor and sensory fibres are enclosed in separate bundles, the latter show marked changes. The sensory group is almost entirely composed of fibro-cellular tissue, in which run congested blood-vessels, and contains hardly any nerve-fibres; those nerve-fibres which remain in this bundle nearly all contain degenerate products.

On the other hand, the motor bundles are filled with their full complement of healthy nerve-fibres.

These points can be excellently seen in both the transverse and longitudinal sections of the nerve-trunks.

In the nerve-trunk, about two inches away from the ganglion, though little or no acute degeneration can be discovered, there is still an undoubted diminution in number of healthy nerve-fibres; two fasciculi contain hardly any nerve-fibres at all, and absolutely none of the others possess their full complement.

Dorsal 12. *Left.*—On this side the peripheral nerve differs markedly from that on the right side, for here all the bundles are well filled with normal fibres.

Dorsal 5, 8, 9, 10 *and* 11. *Right and left.*—Show no change.

Lumbar 1 *and* 2. *Right and left.*—Show no change.

(*d*) *Spinal Cord.*

Method of examination.—Portions of the cord were taken from the levels of entry of all nerve-roots from the 3rd sacral to the 1st cervical inclusive; these blocks were stained by the method of Marchi and cut transversely; several longitudinal sections of portions of the 10th, 11th and 12th dorsal blocks were also made (plate 12, fig. 2).

Dorsal 12.—It has been already noticed that in that portion of the 12th dorsal posterior root of the right side situated between the ganglion and the spinal cord, the morbid change consisted of sclerosis and acute degeneration combined, the former predominating. Now on entering the spinal cord it is to be observed, firstly, that exactly at the point where the pencils of the root penetrate the cord there is a brief length where there is no degeneration at all (as Obersteiner has shown the fibres here are bereft of their medullary envelope); secondly, that as soon as the pencils of the root enter the cord acute parenchymatous degeneration immediately becomes evident and sclerosis is absent or unrecognisable. In transverse sections the degenerated fibres are well seen in the first part of their course cut longitudinally and running for a short distance alongside the inner margin of the tip of the posterior cornu. In longitudinal sections made parallel to the right posterior cornu, the same fibres are beautifully displayed obliquely cut immediately after they enter. In the postero-external columns of the same side transverse sections show some 70 to 100 degenerated fibres immediately opposite the substantia gelatinosa Rolandi. These fibres are derived from pencils of the root which, entering lower down, have at this level assumed a vertical direction. Furthermore, situated in the centre of the right posterior horn, almost midway between the column of Clarke and the caput cornu, is a small isolated bundle of degenerated fibres of delicate calibre; these also seem to have come from the posterior root at a lower level. All these degenerated fibres, both those in the postero-external column and those within the posterior cornu, are well seen in longitudinal section. In the next place, a few fibres of the right anterior root exhibit signs of degeneration in their intraspinal course.

Lastly, scattered all over the field of the right lateral pyramidal tract are degenerated fibres of large calibre, and a few diseased fibres are visible in the left anterior and the left lateral pyramidal tracts. This degeneration is a typical descending one, the result of the lesion in the left cerebral hemisphere described in the autopsy report; it can, of course, be seen in all the succeeding sections, but as it obviously has no association with the herpetic lesion it will not be further alluded to.

Dorsal 11.—In transverse sections the entering fibres of the right posterior root are very different from those of the level last described, little if any degeneration being present in them. The degenerated fibres in the postero-external column are most numerous opposite the substantia gelatinosa Rolandi, but the field in which diseased fibres may be found extends further inwards towards the posterior commissure than it did at dorsal 12. The isolated degenerated bundle in the right posterior cornu is still visible. The anterior roots are healthy.

Longitudinal sections confirm these appearances.

Dorsal 10.—In transverse sections the field in the right postero-external column containing degenerated fibres has considerably altered its position. The outer half is separated by a distinct interval from the posterior cornu, and internally the strip reaches to a point almost opposite Clarke's column, and in this central part the diseased fibres are more densely packed than in the outer portion.

The degeneration in the isolated bundle in the posterior cornu is disappearing, and the entering posterior root fibres look healthy.

Dorsal 9.—The degenerated fibres have shifted their position still further inwards towards the middle line, and are now mainly situated in the inner half of the postero-external column. The strip begins in the neighbourhood of Clarke's column and extends to the periphery, and fibres in the centrally situated part of the strip are again more closely aggregated than those in the peripheral part. The degeneration in the isolated bundle in the posterior cornu has disappeared. The anterior roots are normal.

Dorsal 8.—The fibres in the outer portion of the degenerated strip in the right postero-external column are becoming sparse and scattered.

Dorsal 7.—At this level a small number of fibres at the centre of the strip lie in the outer part of the postero-internal column. At either extremity the strip curves towards the posterior horn.

Dorsal 6.—The degenerated fibres are pushed still further inwards and compared with the sections from Dorsal 11; there is an obvious diminution in their numerical strength. In all about 150 diseased fibres can be counted against about 210 at the lower level.

Dorsal 5.—With the exception of its most peripheral and central parts, the strip is now confined to the postero-internal column.

Dorsal 4.—There is a further diminution in the number of the degenerated fibres. Those situated in the inner half of the strip are again more densely packed.

Dorsal 3.—The strip of degeneration shows signs of being divided into two portions; scarcely any degenerated fibres are visible at its middle, at the periphery a few disseminated fibres are still visible in the postero-external column, and centrally there is a thin strip of diseased fibres reaching almost to the posterior commissure.

Dorsal 2.—At the periphery of Burdach's column there are a few scattered degenerated fibres, and in the inner two-fifths of Goll's column others arranged in a row bordering on the posterior median septum.

Dorsal 1.—Similar to dorsal 2.

Cervical 8.—The number of degenerated fibres has greatly diminished.

Cervical 7.—A minute number of scattered degenerated fibres can be made out in the inner one-third of the postero-internal column, and also at the periphery of Burdach's column. Above this level the degeneration cannot be definitely traced.

Lumbar 1.—The entering posterior roots are healthy, and the posterior columns contain no degenerated fibres. The only degeneration discoverable is in the pyramidal tracts, and this has already been referred to.

Lumbar 2, 3, 4 and 5 show no degeneration referable to the herpes.

Sacral 1, 2 and 3 show no degeneration referable to the herpes.

Case 9.—Richard K., aged 36. Admitted to Claybury Asylum, April 19, 1898. Died February 5, 1899.

SUMMARY.

A typical case of dementia paralytica, developed an attack of herpes zoster over the area in fig. 9. *He died of exhaustion* 153 *days afterwards.*

Microscopically.—The 7th dorsal posterior root ganglion of the right side showed extremely marked sclerotic changes, with destruction of ganglion cells and fibres over that part opposite to the position of the anterior root. No other ganglion was affected.

The corresponding posterior root showed not only some slight *change by Marchi's method, but also evident diminution of fibres by the Marchi-Pal method.*

The spinal cord showed acutely degenerated fibres (Marchi's method), entering at the level of the 7th dorsal root on the right side and passing up in the posterior columns to the level of the 2nd dorsal root.

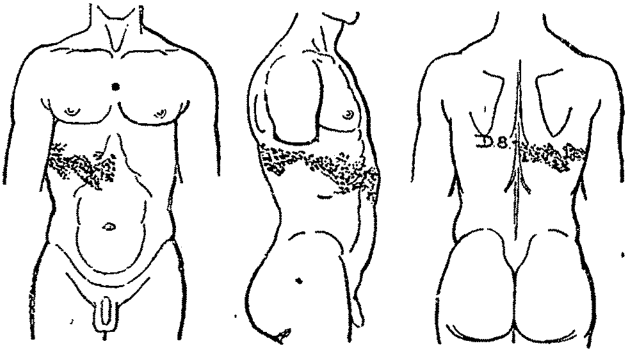

FIG. 9.

To show the distribution of the eruption in Case 9.

On admission he was grossly demented, dull, apathetic and slow of speech. His memory was markedly affected; he knew his name and age, but nothing else. He had no idea of the date, where he was, or how long he had been in the asylum.

His pupils were regular and reacted to light and accommodation. His knee-jerks were not obtained. His gait was slow and tremulous.

On September 6, 1898, he developed a profuse eruption of herpes zoster over the area of the 7th dorsal. The whole area was beautifully marked out as in fig. 9.

By October, 1898, he had become destructive, wet and dirty. His speech was very slow and slurred. His pupils did not react to light. He was much emaciated.

On February 5, 1899, he died of exhaustion, 153 days after the eruption.

POST-MORTEM EXAMINATION.

Twenty hours after death. The body had been kept in the cold chamber from shortly after death until the examination was made.

The body was much emaciated and three deep scars remained to show where the eruption had been situated. The two posterior ones were slightly ulcerated, and looked as if healing had once occurred and the thin deep scar had slightly broken down again.

Brain.—The pia-arachnoid was everywhere adherent.

The convolutions were wasted and the lateral ventricles dilated and granular. The right hemisphere weighed 603 grammes, the left 603 grammes.

The 4th ventricle was granular, cerebellum normal.

Thorax.—The right pleura was adherent at the apex. The apex of the right lung showed several large, active, tubercular foci, but elsewhere the right lung showed broncho-pneumonia with hypostatic congestion of the lower lobe.

The left pleura was adherent at its posterior border. The upper lobe of the right lung was infiltrated with active tubercle, and there was a cavity at the apex of the size of a walnut. The lower lobe was much congested.

Heart normal, aorta slightly atheromatous.

Abdomen.—Liver, spleen and kidneys normal.

MICROSCOPICAL EXAMINATION.

The following parts were examined: (*a*) a series of posterior root ganglia; (*b*) a series of posterior roots; (*c*) the spinal cord.

(*a*) *Posterior Root Ganglia.*

The ganglia examined were the 6th, 7th, 8th and 9th dorsal on both sides. They were hardened in Müller's fluid. A transverse cut was then made through each with a sharp razor, and each ganglion was placed in Marchi's fluid. Each ganglion was embedded in celloidin and cut longitudinally in series. The sections were counterstained by van Gieson's method, by safranin, or by Pal's method.

Dorsal 7. *Right.*—This ganglion shows a remarkable change. Even in the specimens stained by Marchi's method only this change is pronounced, but it is best seen when the sections are counterstained with van Gieson's stain (plate 1, fig. 2B). On that side of the ganglion opposite to the anterior root about one-third of the ganglion obliquely is converted into dense fibrous tissue, in which not a nerve-fibre or nerve-cell can be seen. This focus stains a brilliant red in contradistinction to the somewhat purple interstitial tissue of the normal ganglia, and this is evident even to the naked eye. Thus if sections of the right and left 7th dorsal ganglia counterstained by van Gieson's method are mounted side by side, there is no difficulty in picking out the right ganglion with the unaided eye in consequence of its brilliant red colour. The ganglion of the left side, owing to the presence of the bundles of healthy nerve-fibres and healthy cells, and the absence of dense connective tissue, appears of a purple red colour.

The posterior root and peripheral nerve attached in the longitudinal sections of the right ganglion are converted into fibrous tissue, which also stain brilliant red by van Gieson's method.

Dorsal 7. *Left.*—This ganglion is absolutely normal (plate 1, fig. 2A).

Dorsal, 6, 8 *and* 9. *Right and Left.*—Absolutely normal.

(*b*) *Posterior Nerve-roots.*

Dorsal 7. *Right.*—This root shows no profound degeneration by Marchi's method, but in many places the sheath of the fibres is broken up and swollen, and here and there a few blackly-stained swollen remains of degenerated fibres can be seen. But when stained by the Marchi-Pal method the difference between this root and its companion root on the other side is evident, for the right root shows a marked decrease of fibres. No large deposition of secondary connective tissue is shown by any of the various counterstains employed.

Dorsal 7. *Left.*—This root is absolutely normal.

Dorsal 8. *Right.*—On comparing this root with that of the opposite side there are perhaps fewer fibres. No definite change by Marchi's method.

Dorsal 8. *Left.*—Normal.

Dorsal 9. *Right and Left.*—Normal.

(*c*) *Spinal Cord.*

The cord was hardened in Müller's fluid and stained by the Marchi method. Every segment was then cut and some sections from each segment were stained by Schäfer's modification of the Pal method (plate 11, fig. 3).

Beginning from below upwards, the upper lumbar and lower dorsal segments presented the following appearance:—There was acute degeneration on both sides (Marchi) and a slight amount of sclerosis (Marchi-Pal) in the pyramidal tracts. The posterior column and root zones were entirely free from acute degeneration and sclerosis.

However, at the level of the 8th dorsal root a few black dots are visible in the right posterior horn, which appear to be definite degenerated fibres.

At the level of entry of the 7th dorsal root a mass of degenerated fibres is seen streaming into the cord with the posterior root (plate 14., fig. 1.). One segment higher these fibres are extremely marked, but are now situated entirely in the root zone on the inner side of the posterior horn, and the posterior horn is free from degenerated fibres.

At the level of the 5th dorsal root they are still well seen, but they tend to be separated from the posterior horn by normal fibres. At the level of the 4th dorsal root they diminish in number and become more scattered. At the level of dorsal 3 they are still more diffuse and situated more at the periphery, and at the level of dorsal 1 it is doubtful if any degeneration can be seen.

Throughout the whole of these sections and upwards into the medulla the same degeneration in the pyramidal tracts present below the entry of the affected 7th dorsal root can be seen.

Case 10. — William J., aged 40, admitted to the County Asylum, Rainhill, October 6, 1898. Died July 29, 1899.

SUMMARY.

Suffered from dementia paralytica in a typical form. On October 30, 1898, *an herpetic eruption appeared over the 4th cervical area of the right side (fig.* 10). *Death from general paralysis and phthisis on July* 29, 1899, 272 *days after the attack of herpes.*

Microscopic examination reveals an extensive area of sclerosis in the 4th cervical posterior root ganglion of the right side, evidently the remains of a previous destructive process. In the corresponding posterior root and also in the peripheral nerve there was likewise evidence of sclerosis but no acute degeneration.

The spinal cord showed no acute degeneration.

The spinal cord also shows some tabetic sclerosis, but this does not invalidate the case, as it is due to an affection of lumbo-sacral roots.

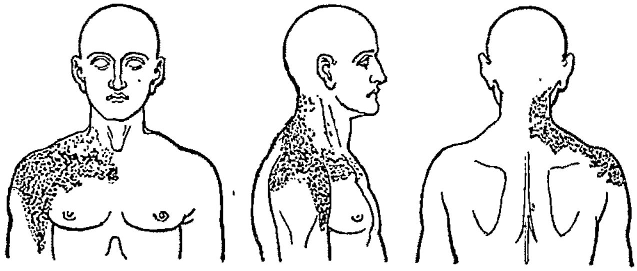

FIG. 10.

To show the distribution of the eruption in Case 10.

History.—Four months before admission he became strange in his manner. He became restless, and would pick up valueless articles, bringing them home and stating they were of much importance. He became extremely erotic, but his wife denied that he had been infected with syphilis. She has never been pregnant. Just before admission to the asylum he had a seizure and the mental symptoms grew worse.

On admission.—He was of slim build and poor bodily condition. His speech was thick with an occasional catch, and face and tongue were tremulous. Pupils small, reacted badly to light. No paralysis.

Mentally he was restless, talkative and excited. He failed to recognise that he was in an asylum and was under the impression that he came there to buy geese that were for sale. He was obviously suffering from dementia paralytica.

Progress.—October 29. He had a typical general paralytic seizure.

October 30. He developed an herpetic eruption over the skin area shown in fig. 10. The vesicles were mainly of small size and were densely distributed over the affected region. Anteriorly the eruption was seen to extend onto the lower part of the area usually occupied by the 3rd cervical, but here the vesicles were sparsely scattered. Excepting at its extreme anterior border the eruption was confined to the 4th cervical area as given by one of us, its posterior or lower border corresponding peculiarly accurately. There was pronounced erythema along with the vesiculation. The temperature was 101° F. (38·3° C).

November 3. The erythema had almost disappeared; many of the vesicles contained pus and scabbing had begun.

December 16. Pustulation had ceased. There was not much scabbing.

April, 1899. He had become extremely demented and physically weak. Seizures occurred occasionally.

July 29, 1899. He died from general exhaustion 272 days after the attack of herpes.

Post-mortem Examination.

The *post-mortem* examination was made fifteen hours after death.

External examination.—Height 71 inches, circumference at shoulders 35 inches, circumference of head $21\frac{5}{8}$ inches. Muscular and osseous development below the average. No local muscular atrophy, but poorly nourished generally.

On the sternum immediately internal to the junction of the 2nd costal cartilage was a pale brown patch of post-herpetic scarring, about 1·5 cm. in diameter. Over the shoulder just in front of the acromion process of the clavicle were three other small patches; a further patch was seen in front of the shoulder joint and another above and external to the joint; lastly, there were two more small patches situated immediately above and below the outer one-third of the spine of the scapula respectively.

The hair was thin but present all over the scalp.

Cranium and Brain.—The calvaria was slightly thickened, and was denser than usual. The lines of the meningeal arteries were rather deep. Greatest transverse diameter of cranium 14·4 cm., greatest antero-posterior diameter of cranium 18·3 cm., cephalic index 78·6 cm.

The dura mater was relaxed frontally and a very thin, brown, non-laminated hæmorrhagic membrane lined the concavity on both sides and extended along the falx and into the frontal, temporal and occipital fossæ. The dura was nowhere abnormally thickened, nor unduly adherent to pia-arachnoid or bone.

The subdural fluid was markedly excessive in quantity and tinged brown in colour. For a general paralytic the large vessels at the base looked remarkably healthy.

There was a moderate degree of opacity of the arachnoid over the convexity of the hemispheres, especially over the frontal lobes.

The pia-arachnoid was moderately thickened, somewhat hyperæmic, and on stripping decortication occurred in patches over the frontal and motor regions.

The cerebral hemispheres were of average size, their form was good and there was no asymmetry. The convolutions were simply disposed and a moderate degree of wasting was noticeable, chiefly in the frontal region. The sulci generally were shallow.

On the under surface of the right temporal lobe close up to the anterior extremity were three minute patches of surface softening; these had brown edges and involved the cortex only. Symmetrically placed on the anterior faces of both first frontal convolutions were two similar, but rather more extensive, patches of softening; these also did not extend below the cortex, and in the subarachnoid space above them brown fluid was collected.

The cerebral cortex was darker than normal, somewhat hyperæmic, distinctly thin, and its striation was indefinite.

The white substance had a normal appearance, but was unduly firm. Enlargement of the lateral ventricles was noticeable, but their ependyma was smooth.

The basal nuclei and other structures presented no naked-eye change. The cerebellar cortex was rather dark and thin, but otherwise there was no noteworthy alteration in this organ, nor in the pons, medulla and remaining intracranial structures.

The encephalon weighed 1,324 grammes, the right cerebral hemisphere unstripped 525 grammes, the left hemisphere 530 grammes, and the cerebellum along with the pons and medulla 162 grammes.

Spinal Cord.—The spinal cord seemed to be somewhat small, and there was an obvious excess of cerebro-spinal fluid, but otherwise there was no naked-eye alteration to note, nor could anything pathological be detected at this stage in the posterior root ganglia and spinal nerves extracted.

Thorax.—Chest narrow. Ribs easily broken. There were old firmly-united fractures of the following ribs on the left side:—the 6th at the costo-chondral articulation, the 7th 1 inch, the 9th 1½ inches, and the 10th and 11th 2 inches external to the costo-chondral joint respectively. On the right side the 11th rib was broken at about its middle. Round all these fractures a considerable amount of callus had been thrown out, and they were supposed to have been fractured prior to admission to Rainhill.

The right pleura was free from adhesions, but on the left side there were adhesions round the apex and along the front of the lung. At the apex of the right lung were a few small patches of caseous consolidation. The organ weighed 15 ozs. (424 grammes). The left lung weighed 42 ozs. (1,188 grammes), it was of increased size and severely diseased. The pleura was thickened and fibrous all over. Along the free margin at the base were several large emphysematous bullæ. On section many large tubercular cavities were found in the upper lobe, and all over the lung were scattered patches of advanced caseous consolidation.

The mucous membrane of the larger bronchi was red and thick, and the bronchial glands were enlarged, while some present caseous foci.

The pericardium was normal.

The heart weighed 6½ ozs. (184 grammes), it was small but of normal shape, its muscle was very firm and of dark colour. Decolourised clot was present in the right auricle, and black clot in the left auricle. There was no valvular disease, but some commencing atheroma, indicated by change of colour and puckering, was noticeable in the thoracic aorta.

Abdomen.—The peritoneum was normal.

The liver weighed 43 ozs., its capsule was thick and white in patches on the convexity, its substance dark and firm.

Gall bladder normal.

Spleen weighed 3 ozs. (85 grammes) and was healthy.

Each kidney weighed 4 ozs. (113 grammes). The capsule peeled cleanly, but the substance was very dark and firm.

The adrenals, pancreas and stomach were healthy.

Along a short length of the small intestine just above the cæcal valve and on and immediately below the valve were about eight small tubercular ulcers, some of which were in quite an early stage of development.

The lymphatic glands of the mesentery were slightly enlarged. The bladder was partially distended with dark urine.

On the dorsum penis immediately behind the corona was a suspicious but indefinite scar (possibly syphilitic).

The left testicle showed a few abnormal streaks on section, which suggested previous orchitis.

The prostate gland and seminal vesicles were normal.

MICROSCOPIC EXAMINATION.

A microscopic examination was made of (*a*) a series of posterior root ganglia, (*b*) a series of spinal nerve-roots, (*c*) the spinal cord.

(*a*) *Posterior Root Ganglia.*

Of the posterior root ganglia the following were submitted to examination:—the 2nd, 3rd, 4th, 5th, 6th and 7th cervical of both sides.

Method of examination.—To prevent error and confusion the individual ganglia, along with that portion of the roots lying central to the body of the ganglion but outside the dura, together with about 5 mm. of the peripheral conjoint nerve-trunk, were taken separately and hardened in different bottles; first in formol 5 per cent. for a week or more, then in alcohol, &c., preparatory to celloidin imbedding. Corresponding pairs from the two sides were then fixed in celloidin side by side on the one block, that from the right side always being distinguished by having a piece of heart-muscle or other distinctive tissue placed alongside it. Serial transverse sections were next cut from one end to the other. To stain these the hæmatoxylin method of van Gieson was employed, and in mounting the finished preparations care was taken to preserve them in strict serial order.

Cervical 4. *Right.*—As this is the only ganglion to show important changes we shall describe it first. There are 175 sections (plate 6, fig. 1B).

Beginning at the central end where the roots pierce the dura, it soon becomes evident that the ventralmost bundle of the posterior root is diseased. It is composed of fibrocellular material instead of nerve-fibres, and the sheath immediately external to it also contains a deposit of small round cells. This diseased bundle can be traced right through all the sections of the roots up to the ganglion, where it runs into a diseased focus which will be presently described. The remaining bundles of the right posterior root, along with the anterior roots of both sides and the posterior root of the left side, are free from noteworthy alteration.

Just before the ganglion begins marked thickening of the sheath of the right posterior root on its ventral side becomes apparent, and is continued through a dozen or more sections.

In section 93 (soon after the beginning of the ganglionic tissue) an obvious focal lesion comes into view. It gradually increases in size and then fades away, and is evident in about forty sections altogether. Where it is well-developed it appears in transverse sections as a large patch on the ventral side of the ganglion, which extends from the surface inwards and involves about one-third of the body. The internal line of demarcation is fairly sharp. The whole of this area is composed principally of wavy fibrous tissue with elongated nuclei, just a few nerve-fibres can be discerned in it, and with the exception of two or three ganglion cells it is completely denuded of these bodies. The sheath overlying this region is not markedly thickened, and the rest of the ganglion has a normal appearance.

The above-mentioned focus of disease extends almost to the distal end of the ganglion, but when the anterior root begins to fuse with the posterior to form the conjoint peripheral nerve trunk, the area of sclerosis soon diminishes in extent. The sclerosis, however, does not cease here, for it is quite clear that the change is continued into the nerve-trunk and that a considerable number of nerve-fibres have been replaced by fibrocellular tissue.

It is obvious from the general appearances that this ganglionic lesion is of considerable standing, and has long passed the acute stage.

One or two small arteries are to be observed in the sheath of the ganglion which have an appearance suggestive of syphilitic endarteritis, but there is no definite histological evidence which will explain the origin of the lesion.

Cervical 4. *Left.*—This ganglion shows no noteworthy change.

Cervical 2. *Right and Left.*—There are one or two syphilitic-looking arteries in the conjoint trunks, but apart from this the ganglia of both sides and their annexa present no change worthy of notice.

Cervical 3, 5 *and* 6. *Right and Left.*—These ganglia are practically normal.

Cervical 7. *Right and Left.*—Almost one-third of the anterior root of the right side appears to be sclerosed. The change is represented by a collection of small round cells and fibrous tissue, and it runs through all the sections.

In the tissues investing the posterior roots of both sides there is an apparent excess of small round cells. This is in all likelihood an early tabetic change.

The Posterior Spinal Nerve-roots.

After preliminary fixation in Müller's fluid the spinal cord in the cervical region was divided up into its eight segments, and to each segment the intradural portion of the roots was left attached. Then after these blocks, with the roots, had been stained by the method of Marchi, certain of the posterior roots, viz., the 3rd, 4th and 5th cervical of both sides, were cut off close up to the cord, care being taken to preserve the bundles in normal relative position. The bundles were then divided into two portions, the peripheral portions were teased, and the central portions embedded in celloidin and cut serially in the longitudinal direction.

Cervical 4.—The posterior root of the right side is practically composed of four main bundles, of which the upper three show no change of importance. A single acutely degenerated fibre is visible here and there, but there is no collection of degenerated fibres, and no evidence of sclerosis.

In the fourth and lowermost bundle there is, however, a morbid alteration, namely, a pronounced disappearance of nerve-fibres and a substitution for them of fibrous tissue. Roughly speaking about half the fibres of this bundle are absent, and the change is as noticeable in the teased preparations as in the serial longitudinal sections. This probably represents the remains of past degeneration.

The 4th cervical posterior root of the left side is also composed of four main bundles, but in none of them is there any noteworthy acute degeneration or sclerosis.

Cervical 3 *and* 5.—The posterior roots of these segments were put to the same searching examination as those of cervical 4, but no change calling for special notice was discovered.

Spinal Cord.

Method of Marchi. Transverse sections.

Cervical 2.—In the centre of the posterior columns there is a wedge-shaped strip of partial tabetic sclerosis. Through the centre of this runs the postero-median fissure, and it practically embraces the whole of the columns of Goll. Its position clearly shows that it originates from disease of roots placed below the cervical region.

In both postero-external columns there are a few scattered degenerated fibres, but there is no degeneration which can be referred to the herpes. The entering posterior root-fibres are free from acute disease.

Numerous acutely degenerated fibres are seen in the direct and lateral pyramidal tracts of both sides, but such degeneration is almost invariably seen in cases of dementia paralytica, and can be attributed to that disease.

Cervical 3.—Shows exactly the same changes as cervical 2.

Cervical 4, 5 *and* 6.—All show similar changes, and nowhere can any change be found corresponding in any way to the herpetic lesion.

Case 11.—Rachel R., aged 64, admitted to Claybury Asylum, January, 1897. Died October 6, 1898.

SUMMARY.

On June 12, 1897, *a typical case of so-called senile melancholia developed an attack of herpes zoster over the* 4*th dorsal area of the right side* (*fig*. 11). *The eruption was extremely profuse, and the whole area was excellently marked out.*

She died on October 6, 1898, 481 *days after the attack of zoster.*

Post mortem.—The axilla showed slight but definite scarring. There were no signs of any disease of the nervous system except such as were due to the zoster.

On microscopical examination the 4*th dorsal posterior root ganglion of the right side showed thickening of the capsule and replacement of a considerable area of ganglionic substance by fibrous tissue. This change occupied that portion of the ganglion opposed to the anterior root.*

The 3*rd and* 4*th dorsal segments of the spinal cord were examined by Nissl's method, and showed no change. The remainder of the cord was normal.*

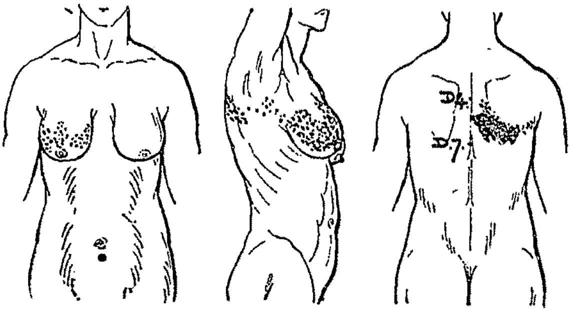

FIG. 11.
To show the distribution of the eruption in Case 11.

On admission she was depressed and inclined to be violent. Memory good. The pupils reacted normally, and knee-jerks were normal. She had no signs of any general nervous disease.

June 12, 1897. She developed an attack of herpes zoster over the 4th dorsal area of the right side (fig. 11), during which she was seen by one of us. Her temperature was 100°. Arteries much thickened. Some emphysema. She was a typical case of so-called senile melancholia.

She died on October 6, 1898, of acute colitis, 481 days after the attack of zoster.

POST-MORTEM EXAMINATION.

Nineteen hours after death. *Post-mortem* rigidity was passing off.

There were no external scars except a few white marks in the right axilla, which may have been produced by the attack of herpes zoster.

There was general œdema and marked congestion of the right lung. The whole upper lobe and upper part of the lower lobe of the left lung were solid with patchy pneumonia. There was much surrounding congestion and œdema.

Heart showed no valvular disease. The muscular substance was fair considering the patient's age. Kidneys and spleen normal. Liver was congested, and showed some fatty change.

Examination of the Nervous System.

The membranes were slightly thickened and opaque over the upper part of the ascending frontal, parietal and paracentral convolutions. There was also some thickening over the cerebellum in the middle line both above and below. Excess of fluid in the meshes of the pia-arachnoid, but the brain could be stripped without difficulty, or the occurrence of decortication. The substance of the brain was normal.

The arteries at the base of the brain showed marked atheromatous changes.

The spinal cord and ganglia showed no naked-eye abnormality.

MICROSCOPICAL EXAMINATION.

The following parts were examined microscopically:—(*a*) a series of posterior root ganglia; (*b*) a series of peripheral nerves close to their entry into the ganglion; (*c*) the spinal cord.

(*a*) *Posterior Root Ganglia.*

The 1st, 2nd, 3rd, 4th, 5th and 6th dorsal ganglia of both sides were hardened in Müller's fluid, embedded in celloidin, and cut longitudinally. The sections were cut in series, and the sections as cut were laid on a glass plate covered with a thin film of collodion. Then a thin film of collodion was poured over the whole, and the double collodion film, between the two layers of which lay the sections in strict series, was detached from the glass plate by laying the whole in alcohol. By this method a series of films was obtained which could be treated by various staining methods, and yet the sections remained in strict series. The staining methods used were the Weigert, Weigert-Pal, hæmatoxylin, hæmatoxylin and eosin, and van Gieson's method.

Dorsal 4. *Right.*—The first sixteen longitudinal sections pass mainly through the capsule and pericapsular tissue. In this tissue a vessel is seen which has undergone marked atheromatous changes. Internal to the muscular coat the wall of the vessel is much thickened, the lumen is irregular and almost blocked. The internal and middle coats are so fused that it is impossible to say how much of this thickening is due to the middle, and how much to the internal layer.

From the seventeenth to the thirty-first section, all of which pass through the substance of the ganglion, the following definite changes are seen. The ganglionic substance is perfect except on that side opposite to the anterior root. Here the substance of the ganglion is adherent to the capsule by firm fibrous tissue. The capsule itself is altered in structure by the substitution of firm connective tissue for the loose wavy layers of which it is usually composed. This condition of scar-formation gradually increases until at last nearly one-third of the substance of the ganglion contains neither cells nor fibres, but is occupied by dense fibrous tissue. The condition closely resembles that found in Case 9, and figured on plate 2, fig. 3.

From the thirty-first to the sixty-sixth section no very definite change can be seen, but with the sixty-sixth section we again find that the sheath is thickened. But here it dips down into the ganglionic substance as a deep pucker, and around this pucker cells and fibres are almost completely absent. This condition extends over about twelve sections and then disappears.

Both these scars lie on that side of the posterior root ganglion opposite to the anterior root, but the first mentioned lies nearer the exit of the posterior roots, the latter nearer the entry of the peripheral nerve. They are probably the remains of a considerable acute lesion probably closely resembling in the acute condition that figured on plate 2, fig. 1.

Dorsal 4. *Left.*—This ganglion is perfectly normal.

Dorsal 1, 2, 3, 5 *and* 6. *Right and left.*—Show no change.

Posterior roots.—Owing to the mistaken method adopted with the spinal cord, no posterior roots could be examined in that region, where they might have been expected to have undergone change.

(*b*) *Peripheral Nerves.*

All the peripheral nerves were normal excepting the nerve that enters the 4th dorsal ganglion of the right side. This nerve seems to have lost fibres, but as these nerves were not cut transversely, the number of fibres lost cannot be counted.

(*c*) *Spinal Cord.*

At the time this case died we were anxious to see if the cells of the spinal cord underwent any change in consequence of the herpetic lesion. The 3rd and 4th dorsal segments were therefore removed at the *post mortem* and placed in 96 per cent. alcohol. They were stained by Nissl's method and various modifications of this method, but showed no abnormality.

The remainder of the cord was hardened in Müller's fluid, and showed neither acute degenerative nor sclerotic changes.

Case 12.—Alice Mary S., aged 20. Admitted to Rainhill Asylum, September 2, 1891. Died July 15, 1898.

SUMMARY.

A female, aged 20, *suffering from congenital idiocy, developed a severe and extensive herpetic eruption over the* 12*th dorsal area of the left side, on February* 15, 1897 (*fig.* 12).

Death from phthisis on July 15, 1898, *one year and* 150 *days after the appearance of the eruption.*

On microscopic examination the following changes were found:—

(*a*) *Posterior root ganglia.—The* 12*th dorsal ganglion of the left side showed a focal lesion. A localised portion of the sheath was markedly thickened and the nerve-cells and nerve-fibres subjacent to this focus were destroyed.*

(*b*) *Posterior spinal nerve-roots.—One small bundle of the 12th dorsal posterior root was partially sclerosed; this bundle could be traced onto the ganglionic lesion just mentioned.*

(*c*) *Peripheral nerves.—No obvious pathological change.*

(*d*) *Spinal cord.—No obvious pathological change.*

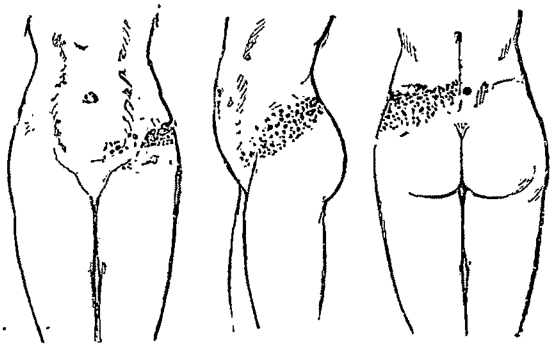

FIG. 12.

To show the distribution of the eruption in Case 12.

History of case unobtainable.

State on admission.—Physically ill-nourished and feeble, and possessed of a delicate frame and poor muscles. Skin healthy. Opacities on both corneæ, but the pupils were equal and their margins regular and they reacted to light and accommodation. Tendon reflexes normal. No paralysis. No heart murmurs. Pulse 120. Chest narrow and deep, no flattening, but distinct dull percussion note at right apex. Teeth good. Alimentary and other systems apparently healthy.

Mentally a complete idiot, unable to express herself in any way. Quite regardless of her surroundings. Wet and dirty and requiring constant attention. Saliva poured continuously from her mouth.

Progress of case.—February 15, 1897. Developed an extensive crop of herpetic vesicles with considerable erythema over the region of the left loin and upper part of the buttock, as indicated in the accompanying fig. 12. The vesicles were largest and most numerous over the anterior part of the iliac crest. A few small scattered vesicles were seen on the abdomen in the iliac region, and posteriorly immediately to the left of the 4th and 5th lumbar and 1st sacral vertebræ some large concrete ones were noticed.

February 22, 1897. Most of the vesicles were purulent, some were scabbing, and the erythema had vanished.

July 26, 1897. The eruption had disappeared and left practically no scarring.

July 1, 1898. Signs of phthisis more pronounced.

July 10, 1898. Rapidly losing weight. Marked dulness over both upper lobes of lungs. Temperature hectic.

Died July 15, 1898, one year and 150 days after the date of appearance of the herpetic eruption.

POST-MORTEM EXAMINATION.

The spinal cord and certain posterior spinal root ganglia and peripheral nerves were extracted twelve hours after death; the full autopsy was performed thirteen and a half hours later. Weather warm and dry.

External appearances.—Body greatly emaciated. Legs and arms slightly drawn up. A circular bedsore over the sacrum, one and a half inches in diameter, denuding the bone. Slight scarring, only visible over the left iliac crest, the sole remains of the herpetic eruption.

Head.—Scalp healthy, calvaria of small size, bone of normal thickness and density. Dura mater well stretched, not abnormally adherent to bone or arachnoid, not unduly thickened. A small amount of black blood clot in dural sinuses. Subdural cerebrospinal fluid present in excess; no blood or membrane.

Brain small, encephalon weighing only 1,154 grammes, but cerebral hemispheres equal and segments proportionately and symmetrically represented. Weight of right cerebral hemisphere, unstripped, 462 grammes; left, 460 grammes. Pia generally anæmic, but of normal density and not adherent. Convolutions of brain arranged on a simple type, the individual gyri small and the sulci rather wide. Cortex pale, firm, anæmic, and reduced in depth. White substance pale and firm; lateral ventricles somewhat dilated and containing an excess of fluid. Basal nuclei normal. Weight of cerebellum 127 grammes, the two hemispheres of equal size, cortex pale and thin, and the white substance pale and firm. Weight of pons and medulla together, 34 grammes; no macroscopic change to note in them, nor in the cranial nerves, nor base of skull.

Spine.—The spinal cord and the posterior root ganglia extracted also showed no naked-eye change.

The vertebræ were healthy.

Thorax.—Some pleural adhesions existed at either apex. Throughout the upper lobes and in the upper parts of the lower lobes of either lung, were scattered patches of consolidation. These patches were to a large extent caseated, and in some small abscess cavities had formed. The right lung weighed 10 ozs. (283 grammes), the left 8 ozs. (226 grammes).

Pericardium healthy. Heart very small, weighing only 3 ozs. (85 grammes), but otherwise normal; auricles contained a small amount of pale blood clot; muscle pale but firm. No organic valvular disease.

Abdomen.—No abnormal adhesions or fluid in peritoneum. Omentum very thin.

The liver weighed 24 ozs. (671 grammes), and though small it looked healthy. Gall bladder normal.

Spleen weighed 2 ozs. (56 grammes), also small, but of good colour and consistence.

Each kidney weighed 2 ozs. (56 grammes); they were small, but the capsule peeled clearly, and the substance was of good colour. Suprarenal capsules healthy.

Pancreas and stomach normal.

In the small intestine a few tubercular ulcers of small size were seen at the lower end of the ileum; the large intestine was healthy.

Bladder distended with thick fœtid urine, mucous membrane swollen and almost black in colour.

Uterus and ovaries healthy.

MICROSCOPICAL EXAMINATION.

A microscopical examination was made of (*a*) a series of posterior root ganglia; (*b*) a series of posterior spinal nerve-roots; (*c*) a series of peripheral nerves; (*d*) the spinal cord.

(*a*) *Posterior Root Ganglia.*

The posterior root ganglia examined were the 9th, 10th, 11th and 12th dorsal and the 1st lumbar of both sides, and the method employed was as follows:—After hardening in Müller's fluid and alcohol in the usual manner, corresponding pairs of ganglia from the right and left sides were taken and embedded in celloidin side by side in one block, special means being employed for distinguishing the right ganglion from the left. Serial transverse sections of the two ganglia were then cut. These were arranged in strict order between two thin layers of celloidin, and stained by the copper-hæmatoxylin method of Weigert. In this manner an examination of and a comparison between corresponding pairs of ganglia was conveniently and effectively carried out.

Dorsal 12. *Left* (*commencing from that end of the ganglion which lies nearest to the spinal cord*).—The first thirty-six sections exhibit no obvious departure from normal. Then follows a point where the ganglionic sheath begins to be markedly thickened, the first indication of a lesion which is continued through all the remaining sections right up to the commencement of the peripheral nerve.

The diseased area as seen on transverse section is situated along the margin of the ganglion on that side of it which is farthest removed from the motor root, to which it lies almost diametrically opposite. The change may be described as follows:—Firstly, the sheath investing from one-fifth to one-sixth of the circumference in this situation is, roughly speaking, three times thicker than it should be, and it possesses a curious homogeneous non-lamellated aspect in marked contrast with the normal wavy appearance of the remainder of the sheath, and even under a high power of the microscope its structure is indefinite. Secondly, the ganglionic nerve-cells and nerve-fibres lying immediately below this portion of thickened sheath to a depth of about ·500 mm. have totally disappeared and been replaced by adventitious fibro-cellular tissue. The dividing line between this destroyed area and the normal remainder of the ganglionic substance is a sharply-defined one. As the peripheral nerve is approached the destruction of ganglionic nerve-cells and fibres becomes less marked, but the sheath thickening remains, and lying outside it is a collection of material having the appearance of organised blood clot in which numerous small round cells and adventitious blood-vessels are visible.

Dorsal 12. *Right.*—There is no change at all corresponding to that described above.

Dorsal 11. *Left and right.*—There is no difference between the two ganglia, and absolutely no focal lesion exists.

Dorsal 10 *and* 9, *and lumbar* 1. *Left and Right.*—Normal.

(*b*) *Spinal Nerve-roots, Anterior and Posterior.*

Stained by the method of Weigert.

Dorsal 12. *Left.*—In the sensory root there is one small isolated bundle which is partially sclerosed, and does not contain its normal complement of fibres. This sclerosed bundle can be traced along to the diseased focus already described as existing in the 12th dorsal ganglion of the left side. The remainder of the sensory root and the whole motor root seem to be healthy.

Dorsal 12. *Right.*—Normal.

Dorsal 11, 10 *and* 9, *and lumbar* 1. *Right and left.*— Normal.

(*c*) *Conjoint Nerve-trunks Peripheral to Ganglia.*

The 10th, 11th and 12th dorsal and 1st lumbar peripheral nerves of both sides were examined most carefully at distances varying from 1 to 20 cm. from the ganglia by the method of Marchi and by the method of Weigert. The former method displayed no acute degeneration whatever, and the Weigert sections revealed nothing in the left 12th dorsal or any other nerve which could be confidently declared pathological.

(*d*) *Spinal Cord.*

As a portion of the spinal cord taken from the 10th dorsal level, and stained by the method of Marchi showed no morbid change it was considered unnecessary to pursue the examination further.

Case 13.—James E., aged 28, admitted to Rainhill Asylum, January 22, 1890. Died March 17, 1900.

SUMMARY.

A chronic demented patient was attacked by herpes zoster on January 9, 1898. *The eruption was distributed in the form of a transversely directed band round the right side of the chest. It began behind opposite the* 7*th and* 8*th dorsal spines, and in front lay immediately below the nipple* (*fig.* 13).

Death occurred from tubercular phthisis on March 17, 1900, 790 *days after the eruption.*

Microscopic examination revealed a distinct lesion in the 6*th dorsal posterior root ganglion of the right side. This lesion had undergone transformation into fibrous tissue in which no nerve-fibres or ganglion cells could be seen.*

In the corresponding posterior spinal nerve-root, and also in the peripheral nerve, several fasciculi of nerve-fibres were sclerosed.

In the spinal cord no acute degenerative or sclerotic changes could be found that could be in any way referred to the ganglionic lesion.

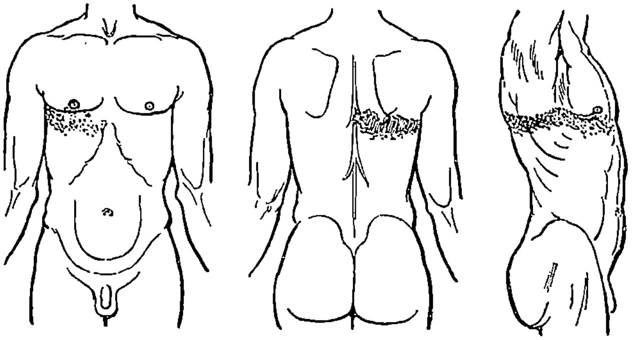

FIG. 13.

To show the distribution of the eruption in Case 13.

Clinical Notes.—Male, aged 28, admitted to Rainhill Asylum on January 22, 1890, on a transfer order from Lancaster Asylum.

No history of the case was obtained.

On admission it was noted that he was of average build, normally nourished and free from physical infirmity.

His mental condition was one of dementia. He was incapable of rendering a coherent account of himself, displayed a marked loss of memory for both recent and remote events, took little interest in his surroundings, was inattentive and unobservant, untidy in his person, and occasionally dirty in his habits.

He remained in this condition throughout his period of confinement, exhibiting no change worthy of record.

On January 9, 1898, he developed a crop of herpetic vesicles, accompanied by much erythema, in the position indicated in fig. 13, made from excellent water-colour drawings, by Mr. Marriott. Viewed from behind the eruption began opposite about the 7th and 8th dorsal spinous processes, and thence extended forwards and slightly downwards in the form of a band fully three inches in width, on a level appreciably below the lower end of the scapula. Gaining the front of the chest this band split up into blotches and streamers; one blotch covered the nipple, but the remainder of the eruption lay below this level. The vesication was soon followed by pustulation, which lasted for a considerable period and left permanent cicatrisation.

On March 10, 1900, it was noticed that he had lost weight during the previous month, but no other alteration in his condition had occurred to attract attention; however, on examination it was discovered that not only was he pyrexic, but also both his lungs were extensively diseased, sharp râles being audible all over them, and cavitation in evidence at the left apex. Diarrhœa was next noticed, and on March 17, 1900, he died, ten years after admission, and 790 days subsequent to the outbreak of the herpetic eruption.

POST-MORTEM EXAMINATION.

The spinal cord and a series of ganglia were extracted twenty-three hours after death, but the full examination was not made until twenty-one hours later, owing to administrative reasons. The weather was cold.

The cadaver was thin but not emaciated, and was below the average in general muscular and osseous development.

No herpetic scarring could be seen on the front or side of the chest, but on the dorsum an inch or more below the angle of the right scapula, and on a level with the spines of the 8th, 9th and 10th dorsal vertebræ, there were several obvious white cicatrices. Otherwise the skin was normal.

Head.—The scalp was healthy and covered by a normal growth of hair. The calvaria was of normal shape, the frontal and occipital bones had an average thickness of 5 and 4 mm. respectively. The lines of the meningeal arteries were plainly marked.

The dura was not unusually adherent to the bone, and was well-stretched. The cerebro-spinal fluid was of normal character, but somewhat excessive in quantity. The dural sinuses were partly filled with black clot. The cerebral veins were engorged with black blood, but the walls of all the larger vessels looked healthy.

The arachnoid was not unduly opaque, and there were no collections of subarachnoid fluid; but the pia-arachnoid membrane, mainly as a result of œdema, was distinctly thickened and soft, and it stripped with great readiness. The pial network of arterioles was injected. The encephalon weighed 1,390 grammes, the right cerebral hemisphere (unstripped) 605 grammes, and the left hemisphere was the same weight as the right. Speaking generally, the brain was of average size, of good shape, and the segments in both hemispheres were proportionately represented. There were indications of slight general atrophy, but no local softening or sclerosis, and the convolutions were somewhat complexly disposed. The cortex in all regions was slightly darker than normal, somewhat hyperæmic, and somewhat reduced in depth, but striation was distinct. With the exception that the puncta cruenta were unduly noticeable, the white matter had a healthy appearance, and was of normal consistence. The ventricles were slightly dilated, but the contained fluid was normal in character, and the ependyma smooth.

The basal nuclei, commissures, &c., showed no naked-eye change. The cerebellum, pons and medulla altogether weighed 182 grammes. In none of these structures, nor in the cranial nerves, was there any alteration worthy of note.

Spine.—During extraction of the spinal cord it was noticed that the vertebræ were abnormally soft, but the cord itself, along with its roots and its membranes, showed no pathological change to the naked eye.

The 3rd, 4th, 5th, 6th, 7th and 8th dorsal posterior root ganglia and several inches of each corresponding peripheral nerve were carefully dissected out, and it was noticed during this process that the nerves on the right side were more adherent to the adjacent pleura than those of the left. (It will be presently noted that the right pleura was extremely adherent all round.)

Thorax.—The intercostal glands on the right side were markedly enlarged. These glands lie quite close, slightly anterior and external, to the posterior root ganglia, and in the normal subject escape notice unless specially searched for. Furthermore, all the fat and connective tissue which invested the ganglia and nerves was darker and more vascular on the right side than on the left, but no special change in any particular ganglion or nerve was discernible.

The right lung weighed 36 ozs. (1,018 grammes), the left 52 ozs. (1,472 grammes). Both were of large size. The right was so tightly adherent all round that it could not be separated with the fingers. The left, however, was separated without great difficulty, but was also adherent all round.

The left pleura was distinctly thickened, the right markedly so.

On section both lungs were practically solid throughout, with the exception of a small portion at each base; but the right lung was more affected than the left. At the apices were several cavities of rather large size, 3 to 4 cm. in diameter; elsewhere were numerous smaller cavities, all with smooth walls and containing yellow pus. Owing to the numerous white caseous foci, sections of the lung had the appearance of gray marble. Many bronchi contained pus, and had a thick red mucous membrane. All the peribronchial glands were enlarged, but they were free from caseation.

There was a moderate excess of pericardial fluid, but no signs of inflammation. The heart weighed 8½ ozs. (240 grammes); it was of normal shape and its muscle was healthy. Both auricles and the right ventricle were full of blood clot. The valves and aorta were normal.

Abdomen.—Peritoneum normal.

Liver weighed 49 ozs. (1,306 grammes). It was slightly paler and softer than natural.

Spleen weighed 5 ozs. (141 grammes), and was rather firmly adherent to the diaphragm. Its substance was abnormally pale.

Kidneys weighed 5 ozs. (141 grammes) and 4½ ozs. (127 grammes) respectively. The capsule peeled cleanly, but the substance was somewhat pale and soft.

Suprarenal capsules, stomach and pancreas were normal.

The jejunum was healthy, but scattered along the ileum was a number of recently-formed, rather small, tubercular ulcers. In the lower two or three feet of the ileum the mucous membrane was in addition reddened, and thickened universally, and the subperitoneal vessels were injected. There was no tubercular ulceration in the large intestine, but in the ascending colon, sigmoid flexure and rectum were numerous simple erosions of the mucosa, occurring in anastomosing lines and circles, such as are often seen in non-tubercular wasted subjects. This condition probably accounted to a large extent for the diarrhœa from which this patient suffered. The fæces were yellow and soft, and the mesenteric glands moderately swollen.

The bladder, penis, testicles, &c., were healthy.

MICROSCOPIC EXAMINATION.

(a) *Posterior Root Ganglia.*

Method of examination.—The 3rd, 4th, 5th, 6th and 7th dorsal ganglia of both sides were all hardened in formalin 5 per cent.; some of these were stained *en bloc* in a mixture of osmic acid 2 per cent. 4 parts, and acetic acid 1 per cent. 1 part, were cut in paraffin and then differentiated as in the method of Pal. Others were cut on a freezing microtome and the sections mordanted in iron alum 2 per cent., stained and differentiated in the solutions of hæmatoxylin and sulphurous acid respectively, used in the method of Pal, and finally counter-stained with alum carmine.

Both these methods display the medullated nerve fibres in a most satisfactory manner.

Dorsal 6. *Right.*—This ganglion was prepared by the second method mentioned above, batches of eight to ten sections being treated at a time and mounted in successive order (plate 6, fig. 2.)

The first few sections show the anterior and posterior roots immediately central to the ganglion. The latter root is composed of two bundles of unequal size, having diameters of ·680 and ·840 mm. respectively. The smaller of these bundles does not contain half the number of nerve-fibres it should and is obviously sclerosed. The anterior root is normal and there is no indication of inflammation in the tissues investing either root.

Nearer to the ganglion the larger of the two posterior root bundles splits into two, while the diseased one remains undivided.

In sections showing the beginning of the ganglion there is no difficulty in following the above-mentioned sclerosed fasciculus; it lies at one side of the field close under the sheath of the ganglion, not far removed from the anterior root. A little further on it can be traced into a focal lesion in the ganglion, which in parts where it is best developed, viz., just distal to the centre of the ganglion, has the following characters. It is recognised as a pale-stained field, occupying about one-sixth of the superficial area of the section and lying immediately below the ganglionic sheath. It extends inwards for a depth of ·595 mm., has an average transverse measurement of ·765 mm., and runs along the circumference under the sheath of the ganglion for a distance of about 1·190 mm. In structure it is composed of a mass of fibro-cellular material, in which the nuclear elements are either round or of elongated form and the fibrous elements irregularly disposed, and it is comparatively rich in blood-vessels, but the most important feature of the area is that hardly a nerve-cell or nerve-fibre of any kind is to be seen in it, showing that the lesion in the first place was of a destructive nature. The periganglionic sheath covering this area is two or three times thicker than normal; it retains its lamellated character but is over-cellular, small round cells being especially numerous on its inner surface. The remainder of the field at this level has a normal appearance, nerve-cells and fibres being present in abundance, and the dividing line between healthy and diseased parts is fairly sharply defined.

Changes like those above described are recognisable in about thirty-five successive sections, and in the sections distal to the lesion a sclerosed area takes its place, which is traceable into the peripheral nerve.

Immediately distal to the ganglion sections show four main bundles of nerve-fibres; one of these is the motor root and the other three constitute the sensory portion of the trunk, and of the latter one fairly large fasciculus, measuring 1·190 by ·765 mm., is severely diseased, being principally composed of fibro-cellular tissue which has clearly taken the place of nerve-fibres. A little further along this sclerosed fasciculus breaks up into three small bundles, and in the end all the above bundles, normal and diseased (including the anterior root) fuse and become surrounded by a common perineurium, but the sclerosed bundle can still be seen lying at one side of the field.

The continuation of the change is described under the heading "*Peripheral nerves.*"

Dorsal 6. *Left.*—The roots seen immediately central to the ganglion are composed of normally stocked fasciculi of nerve-fibres, the ganglionic body is free from focal lesion and the first part of the conjoint nerve-trunk shows no trace of sclerosis.

Dorsal 3, 4, 5, 7 *and* 8. *Right and Left.*—Show no noteworthy change.

(*b*) *Posterior Spinal Nerve-roots.*

Method of examination.—After hardening in formol 5 per cent., the roots were placed for several days in a mixture of four parts of osmic acid 2 per cent., and one part of acetic acid 1 per cent., and were then cut in paraffin. Differentiation when necessary was effected with the solutions employed in Pal's original process for staining medullated nerve-fibres.

By this process the medullated sheath of nerve-fibres of all calibres stains jet black.

Dorsal 6. *Right and left.*—In transverse sections of the root of the right side, two small bundles are seen lying together at one end of the section which are undoubtedly sclerosed, but the number of fibres which have disappeared does not look so great as was expected. However, on comparing the sections of this root with those of the root of the opposite side, one immediately notices that the former is much the smaller of the two, and all things considered, we think it not unreasonable to assume that this root was originally the seat of herpetic degeneration, but on account of the great length of time which has elapsed since the attack of herpes, a considerable amount of contraction has occurred, and this, by diminishing the area of the field of sclerosis, masks and gives a false conception of the actual number of fibres which have been destroyed and absorbed. In the remaining bundles spaces are present which suggest sclerosis.

The root of the left side is normally stocked with healthy fibres. In both roots fibres of large and small calibre are noticeable.

Examination of the 3rd, 4th, 5th, 7th and 8th dorsal roots of both sides gives negative results.

(*c*) *Peripheral Nerves.*

Method of examination.—Same as for the posterior roots.

Dorsal 6. *Right.*—Transverse sections made at a point about 1 cm. distal to the ganglion show that the nerve is composed of five fasciculi, all of approximately equal size, and of these one is seriously diseased. It lies at one end of the section, has a diameter of ·340 mm., and is to a great extent deprived of nerve-fibres, a rough count showing that there are only about 170 fibres present, whereas there is room for six times that number. The fibres which remain are of all calibres, ranging from the ordinary large medullated fibre typical of the peripheral nerve, down through all sizes to the smallest tubule, and the latter are not grouped together in any special manner.

The tissue which has taken the place of the nerve-fibres is of fibrous character, staining of a pale brown tint like the perineurium.

Of the remaining fasciculi one has obviously lost a considerable number of fibres, but of the other three it can only be said that they do not contain quite their normal number.

The perineurium is not altered in any way, either locally or generally, but the blood-vessels which run in it are congested.

In sections about 2 cm. distal to the ganglion the nerve is split up into ten different fasciculi of varying sizes, and of these three bundles lying at one end of the section are undoubtedly deficient in nerve-fibres, and some of the others do not contain their normal number.

In sections about 3 cm. distal to the ganglion the bundles are all smaller and more approximately of equal size. A deficiency in fibres in some of the fasciculi is still noticeable.

In sections 4 cm. distal to the ganglion the nerve is composed of eight fasciculi; of these three fairly large bundles with an average diameter of ·510 mm. lying at one end are fairly healthy. The remaining five bundles, which have an average diameter of ·250 mm., are all sclerosed, and two lying quite at the edge of the section are peculiar in that the fibres which remain are all large, round and swollen, and instead of showing a ring of myelin they stain a uniform jet-black throughout.

In sections 7 cm. distal from the ganglion the nerve consists of one corporate bundle with a diameter of about ·765 mm., in the sheath of which runs a single tiny fasciculus. At one end of this large bundle is an obvious patch of sclerosis involving about one-sixth of its superficial area.

Most of these changes in the peripheral nerve are clearly displayed in the accompanying illustrations, which have been made with an Abbé drawing apparatus, each nerve-fibre being placed in its correct position (plate 16, figs. 3, 4, 5).

Dorsal 6. *Left* (1 *cm. distal to the ganglion*).—This nerve also is composed of five fasciculi all of approximately equal size, and it may be at once stated that no bundle shows any alteration which can be compared with that described as existing in the corresponding portion of the right nerve, but at the same time there are minute spaces scattered about which seem to indicate that a few fibres are wanting. This appearance was also noted in the healthy bundles of the right nerve. There is again no perineural thickening, and the vessels accompanying the nerve are only moderately congested.

Sections about 2 cm. distal to the ganglion show one large, three medium sized, three small and two minute bundles; in none of these is there any pronounced morbid alteration, and the same remarks apply to other sections made at further distal points.

Dorsal 3, 4, 5, 7 *and* 8. *Right and left.*—Show no noteworthy change.

(*d*) *Spinal Cord.*

Method of examination.—One segment only, viz., the 4th dorsal, was stained by the method of Marchi (Orr's modification). The remainder of the cord was hardened in formalin 5 per cent., and sections from various levels were stained with osmic acid and hæmatoxylin by a process which displays medullated nerve-fibres.

Dorsal 4.—As death occurred so long after the herpetic eruption, it was thought that nothing would be gained by examining the cord by the method of Marchi, because traces of acute degeneration which might have been present at an earlier stage would now be absorbed. The sections from this segment prove the correctness of this assumption, for no degenerated products whatever are recognisable in the position in the posterior column which the fibres of the 6th dorsal root of the right side occupy, or indeed in that neighbourhood; but at the bottom of the postero-internal column of the left side, lying close up to the posterior commissure and extending backwards more than half-way up the posterior median septum in the form of a tapering line, the method reveals a curious collection of acutely degenerated fibres, the significance of which is entirely problematical. It is now to be regretted that the cord above and below this level was not examined by the method of Marchi, so that the origin, further course, and destination of these fibres might have been traced.

Also in the left lateral column, scattered about in the direct cerebellar and antero-lateral cerebellar tracts, are some few degenerated fibres, the presence of which is likewise unexplained.

Sections from the 7th cervical to the 3rd dorsal and from the 5th to the 8th dorsal segments inclusive, which were stained to display medullated nerve-fibres, show no definite sign of sclerosis in the posterior columns, and no other pathological change whatever.

The absence of sclerosis in that part of the posterior columns occupied by the fibres of the 6th dorsal root of the right side, proves that post-herpetic spinal degeneration, though plain enough when examined in an early stage by the method of Marchi, is not sufficiently copious to leave behind a recognisable tract of sclerosis after the products of degeneration have been absorbed.

Case 14.—Sydney Herbert B., aged 40. Admitted to the London Hospital (Mr. Jonathan Hutchinson) May 21, 1898. Died July 24, 1898.

SUMMARY.

He suffered from lymphatic sarcoma involving the glands of the neck, axillæ, and groins.

Sixteen days before death herpes zoster appeared over the 4th dorsal area of the right side (fig. 14).

On post-mortem examination many glands were found to be involved, including those of the anterior and posterior mediastinum and the glands on either side of the lumbar spine.

The growth situated on the anterior aspect of the spine in the upper dorsal region had passed in at the foramina, enveloping many of the ganglia and posterior roots on both sides.

On microscopical examination all the ganglia were free from growth, except the 4th dorsal on the right side, which was profoundly destroyed by the invasion of lympho-sarcomatous growth. But although the other ganglia had resisted invasion, the connective tissue around many of those in the upper dorsal region showed new growth in varying quantities, and several roots were affected over and above the 4th dorsal on the right side, which was profoundly degenerated.

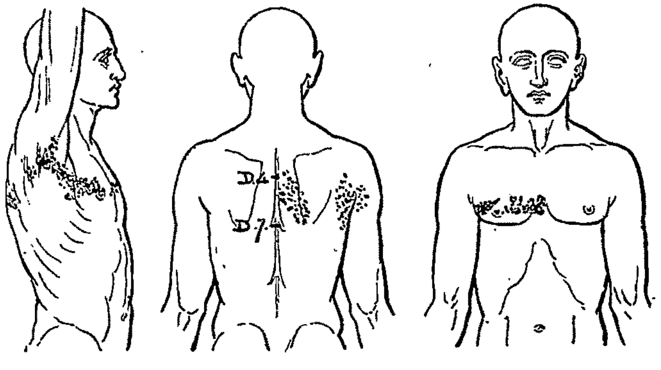

FIG. 14.

To show the distribution of the eruption in Case 14.

History.—He was quite well until six weeks before admission, when he began to feel pain under the shoulder-blades. He put on a mustard plaster, and in the morning the pain had left the shoulder and gone to the small of the back. He continued his work, but felt tired, and the pain in the back still troubled him. He stayed in bed for a couple of days, and then went away from

London. He then suffered greatly with pains everywhere, and could not sit or stand for any length of time. Two weeks before admission the glands in the neck began to swell, but caused no pain. Next the glands in the groin enlarged, and then those in the axilla. The glands were painless, but he suffered from general weakness and pain in the back. Ten days before admission the glands became tender, those in the groin being the worst.

He had always been healthy and strong, except that about three years ago he had some sores in the mouth which came and went in different places. He was put upon mercury, and the sores disappeared.

His mother died of cancer of the uterus, and maternal grandmother of cancer. There was no other family history of importance.

On admission, the glands in both axillæ and in the neck were much enlarged, more so on the left than the right side. The glands in the groin and popliteal spaces were also enlarged, but to a less degree.

There was considerable tenderness of the abdomen, in the region of the liver, and in the lumbar region, but the spleen and liver were not enlarged and nothing abnormal could be felt.

No abnormal physical signs were discovered in the chest.

Urine 1020; contained a small quantity of albumen, but no blood or casts.

His temperature was irregular, but rose to 101° F. (38·6° C.), and rarely fell below 100° F. (38° C.).

Progress.—On June 6 he complained of a sore throat. The left tonsil was inflamed and covered with slough.

Over the 5th rib on the right side, and a little inside the mid-axillary line, a hard lump about the size of a walnut had made its appearance. Other nodules appeared on the ribs, and increased in size and number.

The glands in the neck increased greatly in size, so that they formed almost a collar round the neck.

The tonsil sloughed and the whole tonsillar substance sloughed away.

July 8. He developed herpes zoster over the area in fig. 14, corresponding to and marking out the complete area of the 4th dorsal ganglion. The rash came out quite painlessly.

Rhonchi now began to appear in both lungs.

From this time onwards he wasted profoundly, had occasional attacks of diarrhœa and became very weak.

He died on July 24, seventeen days after the first appearance of the eruption.

POST-MORTEM EXAMINATION.

Twenty-four hours after death. Rigor mortis had passed off. Much wasting. Marked œdema of right leg.

The area that had been occupied by the herpetic eruption was still marked out at the *post mortem* by many scabbed patches.

Bunches of enlarged glands were present in both Scarpa's triangles and on both sides of the neck. They were large, freely movable and on section soft, of a grayish colour and showed no caseation.

The glands of the anterior mediastinum were matted together and invaded by new growth. They formed a large mass, 5 inches (12·5 cm.) from above downwards, 4 inches (10 cm.) from side to side, and 2½ inches (6 cm.) at its thickest part. The growth invaded the upper part of the pericardium and the inner surface of the sternum, opposite the 3rd, 4th and 5th ribs.

There was some enlargement of the posterior mediastinal glands, and the anterior surface of the spine in the upper dorsal region was covered by new growth. This growth dipped into all the foramina.

When the spinal canal was opened from the back and the ganglia dissected for removal, this growth from the anterior surface of the spine was seen in close contact with the ganglia, especially from the 1st to the 5th dorsal. This growth seemed to lie in contact only with the 1st, 2nd and 3rd dorsal ganglia, so that when they were carefully removed the greater part of the growth remained behind in the canal. The 4th dorsal ganglion on the right side was, however, completely lost in the growth, and was therefore removed embedded in the contents of the foramen.

There were no secondary growths in the lungs.

Heart was normal.

In the abdomen there was extreme enlargement of the mesenteric glands, which entirely surrounded, the aorta. A large mass of glands was situated over both iliacus muscles.

The spleen was large and soft, but contained no secondary deposits.

The capsule of the kidneys stripped easily, and on the surface were seen large numbers of whitish-gray masses of rounded shape. These secondary deposits were found, on section, to be diffused throughout the substance of the kidney.

The liver weighed 6 lbs. 2 ozs. (2·77 kgm.). Scattered throughout its whole substance were large white irregularly round secondary deposits. In the right lobe close to the surface was one large secondary nodule of about 1½ inches (4 cm.) in diameter.

MICROSCOPICAL EXAMINATION.

The following portions were examined microscopically:—(*a*) a series of posterior root ganglia, (*b*) a series of posterior roots, (*c*) the spinal cord.

(*a*) *Posterior Root Ganglia.*

The 1st, 2nd, 3rd, 4th, 5th, 6th and 7th posterior root ganglia on both sides were hardened in 96 per cent. alcohol and cut in paraffin in longitudinal series. They were stained by Nissl's methylene blue method and counter-stained with safranin, erythrosin or eosin.

Dorsal 1. *Right.*—The actual ganglion itself is unaffected. The ganglion cells stain well and there is no increase of interstitial tissue and no invasion by small round cells. The capsule is intact, but outside in the periganglionic tissue is a mass of new growth, composed of small round cells that take the blue extremely deeply. These cells lie in spaces resembling those of a lymphatic gland, and the growth is evidently a lymphatic sarcoma.

Dorsal 1. *Left.*—This ganglion closely resembles that on the right side. The growth can be seen around the ganglion, but it has not penetrated the sheath, which is clean and smooth.

Dorsal 2. *Right and left.*—Around both these ganglia a large mass of new growth is visible, but the ganglia themselves show no signs of invasion or of secondary inflammation. The cells stain well.

Dorsal 3. *Right and left.*—On both sides the amount of growth is less and in neither ganglion has the growth penetrated the capsule or caused secondary inflammation.

Dorsal 4. *Right.*—This ganglion shows a completely different condition (plate 2, figs. 1 and 2); for here the thick fibrous sheath of the ganglion has been penetrated by new growth which has involved the ganglionic substance. The space inside the sheath is occupied by a multitude of small round cells that stain extremely deeply with methylene blue. Here and there the remains of ganglion cells can be seen as white or greenish-blue discs with an unstained nucleus. In those specimens where the ganglion has been counterstained with erythrosin, these ganglion cells appear as pink undifferentiated bodies surrounded by masses of small round cells of a deep blue colour. When the inflammation is less intense the ganglion cells stain as uniform blue masses. The more outlying cells show marked chromatolytic changes, Nissl's particles have disappeared, the body of the cell presents a uniform granular appearance, and large light patches are seen in its protoplasm. The nucleus of these cells is excentric, and appear in some cases to have been extruded.

Dorsal 4. *Left.*—Some new growth can be seen in the connective tissue surrounding this ganglion, but it has not penetrated the sheath, and within the substance of the ganglion neither nerve-cells nor interstitial tissue show any change.

Dorsal 5. *Right.*—The ganglion is normal and has not been invaded by the growth which is seen in the surrounding connective tissue.

Dorsal 5. *Left.*—No growth seen. Ganglion normal.

Dorsal 6. *Right.*—No growth seen in the tissue surrounding the ganglion. Ganglionic substance normal.

Dorsal 6. *Left.*—Growth is seen in the connective tissue surrounding the extreme peripheral end of the ganglion. The ganglionic substance is normal.

Dorsal 7. *Right.*—A small amount of new growth is seen surrounding that part where the peripheral nerve gives off its posterior primary division. This growth passes inwards towards the ganglion lying along the side opposite to the anterior root. The ganglionic substance is normal.

Dorsal 7. *Left.*—No growth seen. Ganglion normal.

(*b*) *Posterior Nerve-roots.*

The 2nd, 3rd, and 4th dorsal nerve-roots on the right side all show some degenerated fibres by Marchi's method, but the most marked degeneration is seen in that of the 4th dorsal corresponding to the ganglion that has been destroyed by the new growth. On the left side the 2nd and 3rd dorsal show a slight amount of degeneration, but much less in extent than that in any of the roots of the right side. The 4th dorsal on the left side is normal, and the 5th dorsal on both sides is unaffected.

It must be remembered that although only the 4th dorsal ganglion on the right side was invaded by the new growth, some new growth was seen in most of the foramina surrounding the ganglion and passing inwards with many of the posterior roots. To this must be attributed the degeneration of many roots, although one ganglion only is actually involved.

(*c*) *Spinal Cord.*

The spinal cord was hardened in Müller's fluid, cut, and stained by Marchi's method. Unfortunately, owing to the degeneration of many nerve-roots, the changes in the spinal cord are of but little value from the point of view of localisation. For in the lower lumbar region the cord shows a mass of degenerated fibres in the posterior columns, due to the infiltration of nerve-roots by the lumbar focus of growth (*vide supra* page 480). This degeneration is seen passing up the cord, and at the region of the 6th dorsal has become entirely confined to Goll's column on both sides.

At the level of the 4th dorsal an extremely marked mass of degeneration is seen to enter the cord with the 4th dorsal root on the right side and to occupy the root zone. At the level of the 3rd dorsal this degeneration is extremely marked, and is apparently reinforced by fibres from the 3rd dorsal root. On the left side at this level there are possibly a few degenerated fibres amongst those entering in the posterior root, but the picture presented bears no relation in intensity to that in the root zone of the right side. The entry of acutely degenerated fibres seems to cease at the level of the 1st dorsal, and the degenerated fibres from the 4th, 3rd, 2nd, and 1st dorsal roots take up a position in the postero-external column and can be traced up to the posterior column nuclei.

Case 15.—William H., aged 36. Admitted to the London Hospital under Mr. Moullin, January 26, and died February 13, 1899.

SUMMARY.

On January 26 *he was struck on the back by a descending lift. He was absolutely paralysed below the umbilicus, and sensation to all forms was abolished below the lower border of the* 9*th dorsal segment. Above this level there was a zone of hyperalgesia occupying the* 7*th,* 8*th and* 9*th dorsal areas. The knee-jerks and plantar reflexes were absent.*

February 7. *A small patch of herpes appeared over the* 9*th intercostal space on the left side, close to the tip of the* 9*th and* 10*th rib cartilages.*

He died on February 13, *six days after the development of the eruption and eighteen days after the accident.*

On post-mortem *examination the* 11*th dorsal vertebra was found to have been fractured and the* 11*th and* 12*th vertebræ had gone bodily backwards. A portion of the intervertebral disc between the* 11*th and* 12*th dorsal projected into the spinal canal, cutting the cord like a knife.*

On microscopical examination three separate conditions were found, corresponding with (1) *the direct injury,* (2) *the secondary vascular disturbance,* (3) *the herpetic eruption.*

(1) *The spinal cord was completely divided at the level of the* 1*st lumbar segment. The* 11*th and* 12*th segments also showed hæmorrhages and some infiltration with small round cells. The* 10*th dorsal segment was unaffected by the direct injury, but here and in every segment above, the cord showed the usual ascending degeneration in the posterior and antero-lateral columns.*

The roots of the 10*th and* 11*th dorsal were torn through close to their exit from the ganglion. These ganglia and the portions of the roots attached to them were surrounded by a mass of inflammatory tissue.*

(2) *The cells of all the ganglia examined showed extremely marked chromatolytic changes; Nissl's granules were diminished, the nucleus was excentric and in many places had been extruded. These changes were present even in the* 8*th and* 9*th ganglia, which were entirely free from surrounding inflammation.*

The posterior roots of the 7*th,* 8*th,* 9*th,* 10*th and* 11*th dorsal were more or less congested and showed swelling of the medullary sheath and invasion by leucocytes. These leucocytes contained much material that stained black with osmic acid.*

The whole of these changes are probably due to vascular changes secondary to the injury, and the changes in the ganglion cells are probably associated with the area of hyperæsthesia over the 7*th,* 8*th and* 9*th dorsal areas.*

(3) *The* 9*th dorsal ganglion on the left side showed a small focus of round-celled infiltration. It was the only ganglion that*

showed any such change, and this, taken in connection with other cases, may probably be assumed to be the cause of the eruption of herpes over the tip of the 9th intercostal space.

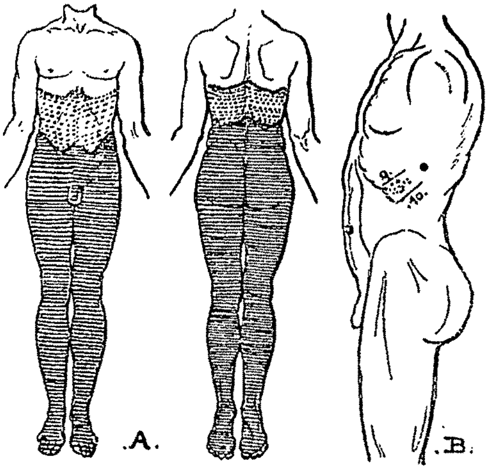

FIG. 15.

A.—To show the area of altered sensation in Case 15. The complete analgesia is represented by horizontal lines, the hyperalgesia by dots.

B.—To show the area occupied by the herpetic eruption in the same case.

History.—At 5.30 a.m. on January 26, he was adjusting the buffers of a lift when it came down, striking him on the back.

On admission.—He was absolutely paralysed in his lower limbs. The muscles of the abdomen about 1½ inches (4 cm.) below the umbilicus were relaxed and flabby, whilst those of the upper abdomen were tense and contracted. Sensation to touch, pain, heat and cold was absolutely abolished above the upper level of the 10th dorsal segment, and the upper level of the loss of sensation was sharply marked, scarcely varying half an inch (1·3 cm.) on repeated testing. Above this level was an area of marked hyperalgesia to all forms of stimulation. Within this band touch, heat and cold all gave him pain, and a moderately painful stimulus became intensely so (fig. 15A).

The knee-jerks were absent on both sides; plantar reflexes absent. The abdominal reflexes were abolished below the level of the umbilicus, but above the umbilicus over the hyperæsthetic area they were distinctly increased.

He had complete retention of urine, and his penis was turgid and semi-erect.

There was a large bruise in the mid-dorsal region over the left side of the spine from above the level of the 8th to the 12th dorsal spine. Several ribs were fractured on the left side.

Progress.—On January 29, the urine became alkaline and remained so until Feb. 5.

On February 7, a small patch of herpetic eruption appeared on the left side over the tip of the 10th rib. It consisted of two small groups, one of twelve vesicles situated over the extreme anterior portion of the 9th space, and a second small group of five vesicles situated over the tip and posterior border of the 10th rib. There was no redness around, and the whole eruption was extremely slight.

His temperature showed an irregular rise and fall, sometimes reaching 102° F. (39° C.), but usually ranging between normal and about 101° F. (38·4° C.). Râles appeared all over the chest, and he died on the early morning of February 13.

POST-MORTEM EXAMINATION.

Made ten hours after death on February 13.

Rigor mortis well marked. No bed sores. Two small patches of herpes were still present over the tip of the 10th rib. No further patches anywhere.

There was a marked projection of the spine in the extreme lower dorsal regions, and on removing the skin the 11th dorsal was found to be the highest vertebra involved in the projecting mass. The spine of the 10th dorsal vertebra was loose and could be moved without difficulty. The transverse processes of the 11th dorsal vertebra were fractured, and permitted movement of the spine in an antero-posterior direction.

On removing the laminæ the 11th and 12th dorsal vertebræ were found to have gone bodily backwards. A portion of the intervertebral disc between the bodies of the 10th and 11th dorsal vertebræ was loosened, and had been forced backwards so as to project, cutting into the cord like the blade of a knife at a level just below the entry of the 11th root into the cord.

At this point the theca was dark red, much swollen and thickened from inflammatory tissue. On the right side the 11th dorsal ganglion was involved in a dense mass of fibrous tissue. From the point where the 10th dorsal root entered the cord on either side the cord was brown and diffluent. At the level of entry of the 11th root it was universally softened, so that the pia-arachnoid contained nothing but blood-stained débris.

The 10th and 11th ribs on the left side had been fractured but had united again, with the formation of a good deal of callus. The point of fracture of the 10th rib was about two inches from its head.

There was a good deal of recent lymph over the base of the left lung. The lower lobe of the left lung was solid. The upper lobe was normal, except for slight bronchitis. The whole upper lobe of the right lung was universally adherent by old adhesions.

Heart, normal.

Liver, large, somewhat fatty.

Spleen, normal.

Kidneys: Capsule stripped with some difficulty. Both kidneys somewhat congested, but otherwise normal.

MICROSCOPICAL EXAMINATION.

(*a*) A series of posterior root ganglia, (*b*) a series of posterior roots, (*c*) the spinal cord.

(*a*) *Posterior Root Ganglia.*

The ganglia were hardened in 96 per cent. alcohol, embedded in paraffin, and cut longitudinally in series. They were stained by Nissl's method and certain series were counterstained with safranin or with eosin.

Dorsal 8.—Both the ganglion of the right and left side show the same changes, and can therefore be described together. There is no thickening or inflammation of the sheath and no infiltration by small round cells in its substance. The vessels are not engorged and there are no hæmorrhages.

But on the other hand the ganglion cells have undergone remarkable changes. In some the Nissl granules are markedly diminished, in others unstained areas are visible. In many the nucleus is excentric, and in some it appears to have been extruded. In such cases the cells are irregular in shape and contain few Nissl-bodies. Thus the ganglion cells of all forms have undergone marked chromatolytic changes.

Dorsal 9. *Left.*—Here the cells have undergone a similar change to that described above, but in addition there is a small focus of small round cells, obviously of inflammatory origin. These cells stain more darkly with methylene blue than the cells of the normal interstitial tissue. There is no sign of a hæmorrhage. If we consider the slightness of the herpetic eruption, we cannot wonder that the amount of inflammatory change was less than in previous cases.

Dorsal 9. *Right.*—This ganglion shows no inflammatory change of any kind; but, just as in all the other ganglia, the ganglion cells show marked chromatolytic changes.

Dorsal 10. *Left.*—This ganglion lay below the fractured vertebra and represents the highest level of the analgesia (*vide* fig. 15A). Under a low power the most marked microscopical feature is the mass of inflammatory tissue that surrounds the posterior root and central portion of the ganglion. The ganglion lies embedded in this tissue like the stone of a fruit. Just central to the ganglion the posterior root fibrils are reduced to a mass of disorganised tissue surrounded by effused blood and inflammatory tissue. Yet, in spite of these profound changes around the ganglion, the sheath has remained intact. The interstitial tissue is quite unaltered, and there is no destruction of ganglion cells from without. But, as elsewhere, the cells themselves show marked chromatolytic changes. These range from rarefaction of the granular staining material to extrusion of the nucleus, with shrivelling of the body of the cell.

Dorsal 10. *Right.*—The destructive process around the ganglion and in the posterior root fibres is not quite so profound as on the other side. But in nature the changes are identical, and here again the sheath of the ganglion has formed a complete barrier to invasion by the inflammatory process.

The peripheral nerve entering both the right and left ganglion is unaffected.

Dorsal 11.—Both left and right ganglia at this level show similar changes. The posterior roots, just after they have left the ganglion, are severed, and the remains embedded in a mass of inflammatory tissue and altered blood. In no case is there the slightest evidence of inflammation within the substance of the ganglia themselves. The cells of both ganglia exhibit profound chromatolytic changes.

The peripheral nerve as it enters the ganglion is in both cases unaltered.

(*b*) *Posterior Nerve-roots.*

The posterior roots were hardened in Müller's fluid and stained by Marchi's method. They were embedded in celloidin and cut strictly longitudinally.

Dorsal 11. *Right and left.*—The fibres of both these roots are swollen and the myelin sheath is in many places interrupted. But the most marked change is the enormous number of leucocytes of all sizes which lie between the fibres. These cells contain large masses of darkly-staining fat or darkly-staining granules. In many places the fibres show marked erosion, and in some places have nearly disappeared under the eroding action of these leucocytes. The vessels are much engorged with blood.

The condition of these roots is unlike that of roots that are undergoing acute degeneration, and the changes they exhibit are probably due to the fact that they were destroyed at the time of the accident. Thus, although the patient lived for a considerable time after the accident, the roots being necrosed could not degenerate, whilst the interstitial tissue would show absorptive changes to an even more marked degree than usual.

Dorsal 10. *Right and left.*—Both these roots show an exactly similar change, but the changes are less marked on the right side than on the left.

Dorsal 9. *Left.*—There is less swelling of the fibres, but the invasion of leucocytes containing particles that stain with osmic acid is extremely marked.

Dorsal 9. *Right.*—This root on the other hand shows no definite change.

Dorsal 8. *Left.*—In parts this root is normal. Then in other parts patches are seen where the above-mentioned changes are visible.

Dorsal 8. *Right.*—Here the change is extremely marked. The central vessel is gorged with blood and all its collateral branches stand out full of blood.

Dorsal 7. *Left.*—This root contains two groups of rootlets. In one of them the vascular engorgement is very marked, and here the above-mentioned changes are present to a marked degree. In the other the vascular disturbance, if present, is slight, and here the swelling of nerve-fibres and leucocytosis is absent.

Dorsal 7. *Right.*—On the whole this root is more normal than that of the other side, but in places the same changes can be seen as in the left root.

Thus the posterior nerve-roots show two changes in this case. Firstly, the 10th and 11th roots on both sides are crushed close to their exit from the ganglion to such an extent that they are practically divided. Here the roots are surrounded by a mass of inflammatory tissue as far as they lie in the canal. The 7th, 8th and 9th roots on the other hand are not divided or crushed, and are not surrounded by inflammatory tissue.

Secondly, all the roots to a varying degree exhibit some changes in the nerve-fibres. They do not show the long bead-like rows of black dots usually seen by Marchi's method in an acutely degenerated nerve. The change consists mainly of a marked swelling of the sheath with erosion and disappearance in parts, accompanied by an invasion of leucocytes of all sizes. These leucocytes are crowded with particles that stain black with osmic acid. Wherever this change occurs in the 7th, 8th and 9th dorsal roots the vessels are engorged, and even the smallest branches are filled with blood.

(*c*) *Spinal Cord.*

The spinal cord was hardened in Müller's fluid, and the 7th, 8th and 9th segments were in part stained with carminate of soda, in part by Marchi's method. The cervical and upper dorsal regions were also stained by Marchi's method. The 11th and 12th dorsal and lumbar cord were cut unstained and then treated with hæmatoxylin and eosin.

From the 2nd dorsal segment upwards the cord shows the typical ascending degeneration, caused by a transverse lesion in the lower dorsal region. The whole of the postero-median (Goll's) column is occupied by degeneration. Degenerated fibres are also seen in the antero-lateral ascending tract on both sides.

Passing downwards the degenerated fibres occupy more of the posterior columns in the usual manner. At the level of entry of the 9th dorsal roots masses of degenerated fibres are seen lying close to the posterior horn on both sides, but the entering roots of the 7th, 8th and 9th dorsal show no acute degeneration.

The 7th, 8th, 9th and 10th segments show no change either by carmine or hæmatoxylin and eosin, but at the level of the 11th dorsal the first signs of traumatic change become visible. Here a small hæmorrhage is visible in the lateral columns close to the posterior horn. Scattered about the cord are many small foci of small round-celled infiltration.

At the level of dorsal 12 the blood clot has expanded into a hæmorrhage destroying one-third of the cord. This hæmorrhage is surrounded by small round cells and the whole cord stains badly, as is usual in these traumatic cases in the neighbourhood of the injury.

At the level of lumbar 1 the cord is completely cut in two, and at the point of division lies a large hæmorrhage in a mass of new tissue.

The remainder of the cord is disorganised and consists of broken down débris enclosed by the pia-arachnoid and some inflammatory tissue.

Case 16.—Amy C., aged 25, admitted to Guy's Hospital December 6, 1897. Died May 28, 1898. (Dr. Pye-Smith.)

SUMMARY.

This patient suffered from a form of meningo-myelitis and multiple sclerosis, secondary to endarteritis obliterans.

In the summer of 1894 *she lost power in the right leg and sight in the right eye. She recovered in six months, except for a little weakness of the left ankle, which came on insidiously during the recovery of the right leg. Then she lost power over micturition. December* 4, 1897, *suddenly lost power in both legs.*

On admission all sensation was lost below the umbilicus, and both legs were paralysed. Complete incontinence of urine and fæces.

February 21, 1898. *She developed an attack of herpes zoster over the area in fig.* 16, *corresponding to the 3rd cervical.*

Motion and sensation somewhat improved; but cystitis reappeared and she died on May 28, *after giving birth to a seven-months' child, ninety-six days after the attack of herpes zoster.*

Post-mortem *examination showed no changes of importance in the abdominal and thoracic viscera, except the signs of old cystitis and secondary abscesses in the kidneys.*

The medulla and spinal cord showed wide-spread sclerosis with acute degeneration around the free border of the sclerotic patches. At the level of the 7th and 8th dorsal the cord was necrosed over rather more than one-half of its extent. There was distinct meningitis and the vessels showed marked signs of endarteritis obliterans.

In connection with the herpetic eruption the 3rd cervical gan-

glion of the left side showed multiple foci of small round-celled infiltration, and the intramedullary portion of the 3rd cervical root was acutely degenerated. The extramedullary roots all showed a curious change, but there was no lesion in them that could be definitely attributed to the herpetic foci in the ganglion.

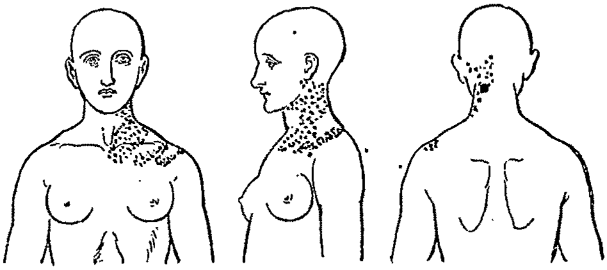

FIG. 16.

To show the distribution of the eruption in Case 16.

History.—In the summer of 1894 she was seized with shivering whilst out walking one evening, and for the next two days suffered from headache, languor and depression. On the third day she found that her right leg was weak, cold and seemed to have lost feeling. Next morning the leg was absolutely paralysed. She remained in bed three months, and during this time she gradually lost the sight of the right eye. Vision returned suddenly after three weeks, but she then saw objects double at a distance. At the end of three months she began to regain feeling in the right leg, and in six months from the onset was able to walk two or three miles.

During the early months of 1895 she was quite well, except that she noticed some weakness of the left ankle, that persisted up to admission.

For eighteen months before admission she had some difficulty in holding her water. This varied from day to day, and at times became complete incontinence.

With exception of the weakness of the left ankle and the difficulty in holding her water she remained well until December 4, 1897. At 5 p.m. on this day she came downstairs, and coming quickly into the room suddenly fell onto the floor, but did not hurt herself. She found she was quite unable to move her legs. She had no pain, but had lost all feeling in the legs.

She was brought to Guy's Hospital on December 6, 1897, and *on admission* her condition was as follows :—

She was a sallow, extremely dark-complexioned woman of 25. Bright and intelligent.

She lay in bed unable to move her legs or change her position, but she could use her arms.

Nervous system.—Speech unaffected. No headache. No fits. There was complete paralysis of both legs and of the lower part of the trunk, with spastic rigidity. No wasting or change in electrical reactions.

There was no weakness, tremor, or inco-ordination of the upper extremities. She could pick up a pin easily with either hand.

There was complete loss of touch, pain, heat, and cold in both legs and over the front of the abdomen up to a level about six inches above the umbilicus. Posteriorly the total anæsthesia and analgesia reached up to the level of the 11th dorsal spine. The upper level, both in front and behind, varied within considerable limits on different occasions. Above this area of lost sensation was a band of hyperæsthesia extending upwards to the level of the 5th space.

The knee-jerks were not obtained, and there was no ankle clonus. The elbow-jerks were present. The plantar reflexes were exaggerated and the right was greater than the left. The abdominal reflexes were not obtained.

The pupils reacted to light and accommodation. There was no ocular paralysis. The face moved well and equally. No difficulty in swallowing. The tongue moved well and was not wasted.

Hearing, smell, and taste were normal. The discs were said to be perfectly healthy.

She had lost all control over both urine and fæces.

The urine was acid and contained no albumen or sugar.

Progress.—On December 16 the knee-jerks were noticed to have returned, but there was no ankle clonus.

On February 21, 1898, she developed an attack of herpes zoster over the area in fig. 16. Owing to the kindness of Dr. Pye-Smith one of us was permitted to see her and to take full notes of her condition.

At this time she showed complete spastic paraplegia of both legs and voluntary movement was impossible either at or below the hips. There was no loss of power in the arms or hands. No tremor or wasting.

On the right half of the body sensation to touch, pain, heat, and cold was absolutely lost up to a line corresponding to the upper border of the 7th dorsal area. On the left side light touch and pain stimuli were lost up to the lower border of the 9th dorsal, heat and cold up to the lower border of the 7th dorsal. On the left side the 8th and 9th dorsal areas were occupied by a band of hyperalgesia. Deep touch was present over the whole of the left side, even to the sole of the foot.

The knee-jerks were now enormously increased and well-marked ankle clonus was obtained on both sides. The plantar reflexes were increased.

The pupils reacted to light and accommodation and there was no ocular paralysis. Undoubted nystagmus was present when she looked to the left, but not when she looked upwards, downwards, or to the right. Movements of the face were good and the tongue was unaffected.

She complained that her vision was failing again, and the left disc was distinctly paler than the right, but not to an extent that could make the diagnosis of optic atrophy certain.

There was still complete loss of control over both urine and fæces.

On March 5 she could feel a faradic current on the lower part of the right abdomen and over the right thigh for the first time since admission. By March 21 she could move the left leg slightly, and touch could be felt all down the front of the left leg, but painful stimuli were not appreciated as before. By April 22 she could move both legs, and sensation had still further improved.

On May 27 she gave birth to a child weighing 2 lb. 2 oz. (1 kgm.), apparently a seven months' fœtus, which died the same night. She was much collapsed, refused food, and died on May 28, ninety-six days after the outbreak of herpes zoster.

Post-mortem Examination.

Owing to Dr. Perry's kindness, one of us was permitted to make an examination nineteen hours after death.

Marked scarring was present within the area that had been affected by the herpetic eruption, and some of the scars were still scaly.

Both pleural cavities were normal, and the lungs were healthy, except for some hypostatic pneumonia of the upper part of the lower lobe of the left lung.

The pericardium was normal. There was no abnormality in either the muscle or valves of the heart.

The liver was normal.

The spleen was normal.

The bladder showed signs of chronic cystitis, especially about its neck.

Both kidneys contained small secondary abscesses, but there was no marked pyelitis.

The uterus was enlarged and contained no remains of placenta. The placental site looked healthy.

The large vessels were healthy to the naked eye, but subsequent microscopic examination showed that the smaller vessels of the nervous system had undergone extensive changes. The smaller cerebral vessels were markedly thickened by overgrowth of the endothelium, and in places were almost obliterated by nodular thickening. The vessels of the cord, especially in the region of the necrotic area, showed distinct nodular endarteritis.

Examination of the Central Nervous System.

The brain showed no naked-eye abnormality. Horizontal and vertical sections failed to reveal any localised patches of softening.

The pons and cerebellum showed no marked changes.

On removing the spinal cord and medulla it was at once obvious that they were the seat of profound changes. The cord was diminished in size, especially in the mid-dorsal region, and pale yellowish-white streaks could be seen running longitudinally up and down the cord. This appearance was most evident to the naked eye in the centre of the posterior columns and in the posterior aspect of the lateral columns.

The posterior and anterior roots and the posterior root ganglia showed no naked-eye changes.

MICROSCOPICAL EXAMINATION.

An examination was made of (*a*) a series of posterior root ganglia; (*b*) a series of posterior roots; (*c*) the spinal cord.

(*a*) *Posterior Root Ganglia.*

The ganglia were hardened in 96 per cent. alcohol, embedded in paraffin, and cut in series. The ganglion of the right and of the left side, at each level, were embedded in the same block and cut and stained together, so that each section of the paraffin block contained a section of the right and one of the left ganglion at the same level.

The sections were stained with methylene blue according to Nissl's method, and counterstained with erythrosin.

Cervical 2.—On neither side is there any change in the interstitial tissue, nor infiltration by small round cells. But on the other hand, the ganglion cells do not stain well with methylene blue. The cells are unaltered in shape and the nucleus is not excentric, but they show a tendency to pick up the erythrosin rather than the methylene blue. This tendency is perhaps more marked in the ganglion of the left than on the right side, but we do not consider it has any direct bearing on the herpetic lesion.

Cervical 3.—These ganglia were cut longitudinally.

Cervical 3. *Left.*—There is a remarkable difference between the condition of the interstitial tissue in the ganglion of the left and that of the right side. (Plate 4, figs. 1 and 2). Scattered throughout the ganglion of the left side are numerous foci of round cells which stain deeply with methylene blue. The ganglion cells stain less deeply on the left than on the right side. Thus, where the ganglion is under-stained with blue the ganglion cells are seen to have taken the erythrosin, and the only blue is seen in the still darkly-stained small round cells. In the neighbourhood of these foci of darkly-staining small round cells the ganglion cells do not stain at all and in places appear to be disintegrated. They are not vacuolated, and the nucleus is not excentric, but they are in such a condition that the body of the cell and the nucleus stain red (with erythrosin), only the nucleolus taking the blue. No hæmorrhages are visible.

Cervical 3. *Right.*—The ganglion cells do not stain well with methylene blue, but there are no foci of darkly-staining small round cells, as on the left side.

Cervical 4.—On neither the right nor the left side is there any change in the interstitial tissue. In fact, these ganglia are normal, excepting that the ganglion cells do not stain well.

Cervical 5.—Both right and left ganglia are normal. The cells stain better than in the other ganglia and there is no interstitial change.

(*b*) *Posterior Nerve-roots.*

The roots of cervical 2, 3, 4 and 5, on both the right and left side, were hardened in Müller's fluid and stained by Marchi's method. They were then cut longitudinally. Several roots were also examined in the dorsal region by the same method.

None of them show any signs of acute degeneration by Marchi's method, but the fibres do not stain well. They are pale and ash-gray coloured, their outline is indistinct, and many of them are slightly swollen. The demarcation between axis cylinder and fibre is not clearly marked. Although none of them show clearly-marked Marchi's degeneration, leucocytes containing fat and many irregular fat globules are seen lying between the fibres.

These changes are not more evident in one root than in another, and bear no relation to the herpetic lesion. For they are equally present in the cervical roots and in those of the dorsal region.

Thus the changes in the posterior nerve-roots seem to depend on the general disease rather than on the herpetic lesion.

(*c*) *Spinal Cord.*[1]

The spinal cord was hardened in Müller's fluid and stained by the Marchi, Marchi-Pal, and Stroebe methods, and also with hæmatoxylin and eosin.

The condition of the spinal cord is best understood by beginning from below and working upwards.

At the region of the 4th lumbar a wedge of sclerosed tissue runs inwards on either side in the postero-lateral region of the cord. At the level of the 1st lumbar these areas have spread forwards and increased considerably in depth. They are accompanied by many degenerated fibres (Marchi) where they abut on the remainder of the cord. There is some scattered acute degeneration in the posterior columns.

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[1] A full description of this case will be included by Mr. A. F. Tredgold in his paper on "Sclerosis of the Nervous System."

At the level of the 8th dorsal the whole anterior portion of the cord is necrosed and converted into a mass of granular débris, in which can be seen the remains of thickened and blocked vessels. In that part of the cord which still remains partly recognisable large and dense patches of sclerosis can be seen. Yet even in this portion, profoundly degenerated as it is, Weigert's method shows a number of blue fibres between the sclerosed patches, showing that all continuity is not destroyed.

At the level of the 7th dorsal this process has gone even further. The whole anterior part of the cord is necrosed, and the thickened membrane enclosing the debris of corpuscles and broken-down nerve-fibres contains thickened vessels and distended lymphatics. One large vessel is completely blocked. But at this level there is a definite line of demarcation between the necrosed anterior portion and the sclerosed posterior and postero-lateral portions of the cord.

At the level of the 6th dorsal the cord is much diminished in size, but is not necrosed. Patches of sclerosis are seen in the posterior columns, the postero-lateral columns, and anterior columns. All these patches are surrounded by much acute degeneration (Marchi).

From the 4th dorsal upwards the cord has nearly regained its usual size, but the patches of sclerosis in the posterior columns and in the lateral columns are very prominent. That portion of Goll's column which is not sclerosed shows acute degeneration.

At the level of the 3rd cervical similar appearances are present, but there is a field of acute degeneration representing the incoming root on the left side.

Further up the cord, at the level of the 2nd and 1st cervical, this field is seen lying close to the posterior horn.

Thus, in conclusion, the spinal cord shows the following different conditions:—

(1) An acute necrosis secondary to vascular obliteration.

(2) Areas of sclerosis which are not confined to tracts, also apparently secondary to partial vascular occlusion.

(3) Areas of acute degeneration on the extending border of these patches.

(4) Possibly some ascending and descending degeneration secondary to the focus of almost complete transverse division (dorsal 7 and 8).

(5) Acute degeneration entering the cord with the 3rd cervical root, probably connected with the herpetic lesion of the 3rd cervical ganglion on the left side.

(6) Meningitis of the membranes surrounding the cord, particularly on the anterior surface. These thickened membranes contain obliterated, or partly obliterated, vessels.

Case 17.—Joseph W., aged 56. Admitted to Rainhill Asylum March 15, 1898. Died September 14, 1898.

SUMMARY.

Admitted for general paralysis of the insane.

On June 6, 1898, *herpes appeared over cutaneous area of* 8*th dorsal segment on the left side* (*fig.* 17).

Death took place from dysentery 100 *days afterwards.*

All the posterior root ganglia were healthy except the 8*th dorsal of the left side. In this ganglion the sheath was thickened and there was an inflammatory focus causing destruction of some few ganglion cells.*

The spinal cord showed the changes of early tabes. In addition a mass of acutely degenerated fibres entered the cord at the level of the 8*th dorsal root on the left side.*

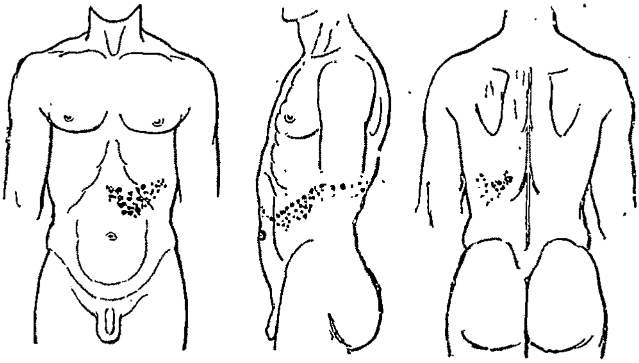

FIG. 17.

To show the distribution of the eruption in Case 17.

History.—Married; one still-born child and two which died when two days old. Syphilis admitted. Occupation, a marine engineer. Had had malaria in Africa several times. During the last three years had complained of general weakness and had twice been in hospital. Temperate as regards drink.

On admission.—Of slim build but fairly well nourished. No paralysis of motion or sensation. Speech clear and distinct. Gait good, but arm movements not under perfect control. Facial tremor. Knee-jerks absent. Superficial reflexes obtainable. Pupils small, but equal; they hardly reacted to light, if at all. Tongue protruded straight, almost free from tremor. Circulatory, respiratory, alimentary, and genito-urinary systems normal. General condition fair. Mentally restless, interfering, talkative, and the subject of grandiose delusions.

Progress.—June 6, 1898. Developed a mild herpetic eruption on skin of trunk, in region indicated (fig. 17). The vesicles were all of small size and were not numerous anywhere; there was practically no erythema and no constitutional disturbance.

June 13, 1898. Some of the vesicles had disappeared, some were scabbing, and others were pustular.

July 1, 1898. The eruption had disappeared and left but slight pigmentation.

He deteriorated mentally and physically, and on August 17, 1898, had several seizures of a mild type in rapid succession.

September 1, 1898. Developed dysenteric diarrhœa with pyrexia and prostration. This resisted treatment, and he died September 14, 1898, 100 days after the appearance of the eruption.

POST-MORTEM EXAMINATION.

Examination twenty-one hours after death. Warm weather.

Tall, slim frame, poor musculature. Just a trace of brown pigmentation over area where the herpetic eruption had been distributed. Skin otherwise clean.

Scalp and cranium normal.

Dura mater slack frontally, not thickened nor adherent. Sinuses partly filled with blood clot. Subdural fluid greatly in excess, no blood or membrane. Larger arteries sclerosed.

Pronounced general arachnoid opacity, Pacchionian bodies slightly enlarged.

Pia mater distinctly thickened and moderately hyperæmic; it stripped in one sheet, but tended to cling in the sulci. No decortication.

Cerebral hemispheres of fair size and symmetrical. Indications of general atrophy. Sulci wide.

Right hemisphere unstripped weighed 592 grammes, left hemisphere 607.

Cortex dark, hyperæmic, thin; striation indistinct.

White matter normal. General consistence firm.

Lateral ventricles enlarged, fluid in excess, ependyma granular.

Basal nuclei healthy to naked eye.

Cerebellum weighed 140 grammes. Cortex dark and thin.

Pons and medulla together weighed 35 grammes. No focal lesions. Ependyma of 4th ventricle granular.

Pituitary body, pineal gland, cranial nerves, &c., healthy to naked eye.

Vertebræ normal.

Fluid in spinal canal in excess.

The spinal pia-arachnoid was thicker than normal all along, but this was particularly marked on the dorsal aspect of the cord. Furthermore, there were firm fibrous adhesions between the dura mater and the pia-arachnoid, covering that length of cord which lay between the levels of origin of the 3rd and 11th dorsal nerves. This was entirely confined to the dorsal side; there were no adhesions worth mentioning on the ventral aspect. Sections of the spinal cord revealed no macroscopic abnormality.

A series of posterior root ganglia and spinal nerves which were extracted also looked healthy to the naked eye.

Old fibrous adhesions were present round the upper lobe of right lung. Emphysema anteriorly in both, and on section general œdema and congestion, with a few patches of lobular pneumonia posteriorly. Bronchi congested.

Pericardium healthy. Epicardium dull gray in colour. Muscle dark and firm. No organic valvular disease.

Peritoneum normal. Liver of normal size and shape, dark and firm on section.

Weight of spleen 3 oz. (85 grammes), small but healthy on section.

Right kidney weighed 5 oz. (141 grammes), left 8 oz. (226 grammes); capsule peeled cleanly, substance dark and firm, cortex of normal depth.

Suprarenal capsules, stomach and pancreas healthy.

Small intestine œdematous, but otherwise normal.

The last foot of the large intestine was gravely diseased; the wall, including mucosa, submucosa, muscle and serosa, was markedly thickened. The mucous membrane was coated with a thick gray slough or pellicle, and in places this was eroded and the submucosa laid bare; there was no deep ulceration, and the rest of the large intestine was normal. The contents of the large bowel were fluid and of light yellow colour.

The glands into which the lymphatics from the rectum and sigmoid flexure empty were red and enlarged.

Bladder normal. Prostate normal. Left testicle fibrotic.

MICROSCOPIC EXAMINATION.

The following parts were submitted to examination: (*a*) a series of posterior root ganglia with attached roots and peripheral spinal nerves; (*b*) the spinal cord.

(*a*) *Posterior Root Ganglia.*

The posterior root ganglia examined were the 6th, 7th, 8th, 9th and 10th dorsal of both sides.

The method employed was as follows: All were primarily fixed in formalin 5 per cent. and afterwards hardened in alcohol. Corresponding pairs from opposite sides were then embedded in celloidin in juxtaposition, special means being employed for the identification of the right ganglion. The pairs of ganglia were then cut transversely, in strict series, no sections being thrown away.

The sections of the 6th and 7th ganglia were stained in Ehrlich's acid hæmatoxylin, those of the 8th, 9th and 10th ganglia by the hæmatoxylin fuchsin method of van Gieson, modified as follows: instead of Delafield's hæmatoxylin Ehrlich's acid solution was employed, and both after staining with hæmatoxylin and after the treatment with the picric acid and fuchsin solution, the sections were washed in dilute lithia water instead of plain water. This was found of advantage in so much as it intensified the blue or purple tints, prevented overstaining with fuchsin, and also accelerated the process.

Dorsal 8. *Left.*—Beginning at the central end of the series, the spinal nerve-roots show grave alteration. The change is bilateral, and does not affect the actual bundles of nerve-fibres so much as their investments. The sheath of pia mater, which is reflected on to them from the spinal cord, presents a general inflammatory thickening and is densely infiltrated with small round cells (in places there are large collections of these bodies), and in many instances the inflammatory exudation has penetrated the perineurium of individual nerve-bundles and given rise to changes in them. Thus the anterior and posterior roots have the appearance of being glued together by an inflammatory material. Wherever blood-vessels are present they are congested, and in some instances they are surrounded by hæmorrhagic extravasations. The next twenty sections show no noteworthy change, but thirty to forty sections from about the centre of the ganglion exhibit an alteration of the sheath which must be regarded as pathological. Running round about one-sixth part of the circumference of the sheath, and lying mainly on and without it but partly within its lamellæ, is a dense layer or collection of small round cells, about as deep as the sheath itself. The portion of sheath affected lies not far removed from the motor root. We are forced to look upon this alteration as pathological, because such a change is not to be seen in the corresponding ganglion of the opposite side, nor in any other of the ganglia from this case which we examined. But at the same time it is not quite like the ganglionic lesion which we have discovered in other cases of herpes; for the nerve-cells which lie immediately subjacent to the portion of thickened sheath are apparently left intact, at any rate they are certainly not destroyed *en masse*, as they generally are, and though their nutrition may have been interfered with, the only positive evidence thereof is the presence among them of a few foci of small round-cell proliferation in the neighbourhood of the blood-vessels.

The remaining sections of this ganglion show no change.

Dorsal 8. *Right.*—This ganglion differs markedly from the 8th dorsal ganglion of the opposite side. For although there is a similar perineural inflammation around the posterior root, all signs of inflammation cease some distance before the ganglion is reached. Moreover, the sheath of the right ganglion shows no signs of thickening, and there is no inflammatory focus corresponding to that in the ganglion of the left side. The cells of the right ganglion are, as far as can be seen by the modified van Gieson method employed, quite normal in number and distribution.

Dorsal 7. *Right and left ganglia.*—The inflammatory change round the nerve-roots noticed in dorsal 8 is almost absent, and the sheath and substance of these ganglia are normal.

Dorsal 6, 9 *and* 10. *Right and left ganglia.*—Sheath and substance of the ganglion show no abnormal change.

Spinal Cord.

Stained by Marchi's method, and transverse sections cut at the level of entry of the 10th, 9th, 8th, 7th, 6th, 5th and 1st dorsal, and 7th cervical nerve-roots. (Plate 12, fig. 3.)

Entry of dorsal 8.—A few definitely degenerated fibres enter the cord at this level from the left posterior root. They appear as lines of black masses just internal to the tip of the posterior cornu, and in sections through the upper part of the segment; the same fibres are seen a little further in cut transversely. This degeneration is to be referred to the lesion in the left 8th dorsal ganglion.

In addition to this acute degeneration, there are two strips of partial tabetic sclerosis symmetrically disposed in the posterior column, one of which is situated along the line of junction of the columns of Goll and Burdach, and the other borders the posterior median septum. These areas are only partially sclerosed, for some healthy fibres can be seen throughout them. In the lateral pyramidal tracts of both sides, and also in the direct pyramidal tracts, disseminated, acutely degenerated fibres of large calibre are to be seen, the right anterior and the left lateral tracts being especially affected. This degeneration is referable to the general paralysis from which the patient suffered.

Dorsal 7.—No acutely degenerated fibres enter at this level, and those seen in the last section lie as a strip adjacent to, but not quite touching, the outer one-third of the posterior cornu. The diseased fibres are of medium calibre and their total number does not exceed seventy.

The pyramidal degeneration and the tabetic sclerosis abovementioned are still present, but as they can have no connection with the herpes no further reference will be made to them.

Dorsal 6.—The degenerated fibres in the left postero-external column are slightly further removed from the cornu, and the dorsal extremity of the strip approaches the periphery.

Dorsal 5.—The number of acutely diseased fibres is sensibly diminishing.

Dorsal 1.—An extremely delicate, but, at the same time, distinct strip of degenerated fibres is visible in the left posterior columns running from the periphery downwards in the direction of the posterior commissure, along the line of junction of the columns of Goll and Burdach. The same strip is not recognisable in the right posterior columns.

Cervical 7.—The degenerated strip seen in the left posterior columns at dorsal 1 is still just discernible; it has now gained the postero-internal column.

Thus the microscopic changes found in this case may be summed up as follows:—

All the posterior root ganglia were healthy, excepting the 8th dorsal of the left side, which showed a local thickening of the sheath at about its centre. The proximal extremity of the ganglion was also involved in an inflammatory lesion which had caused destruction of some few ganglion cells.

Of the posterior roots examined several, viz., the 6th, 8th, 9th and 10th of both sides, were affected by a tabetic inflammatory process, and in the posterior columns of the cord also were signs of early tabes.

A number of acutely degenerated fibres entered the spinal cord by the 8th dorsal posterior root of the left side, forming a field of degeneration that followed the usual course.

At first sight it would appear that this case was vitiated by the co-existence of the tabetic process; but in reality it was thereby rendered more instructive. We know that it is uncommon in an ordinary case of tabes dorsalis to find prominent inflammatory changes in the posterior root ganglia. But at the same time the occurrence of herpes in cases of tabes dorsalis is a recognised clinical fact, and it is probable that in such cases the inflammatory process in the posterior roots peculiar to tabes spreads to the posterior root ganglion and so determines the herpetic eruption. We believe that the above case is an illustration of this condition.

That the 8th dorsal ganglion of the left side would, in this instance, be only slightly diseased, was to be expected from the mild and scattered form assumed by the eruption; but the fact that it was the only ganglion diseased, coupled with the typical acute spinal degeneration entering at the 8th root, renders the case confirmatory from the point of view of localisation.

Case 18.—Percy Matthew T., aged 31. Admitted to Rainhill Asylum, October 15, 1896. Died October 12, 1897.

SUMMARY.

Admitted to Rainhill Asylum suffering from general paralysis of the insane. Speech slurred. Knee-jerks exaggerated. Pupils react sluggishly to light. Tongue tremulous.

On September 12, 1897, *a herpetic eruption appeared which involved the skin of the chin and cheek of the right side of the face (inframaxillary division of 5th nerve)* (*fig.* 18). *Death occurred from general paralysis on October* 12, 1897, *thirty days after the appearance of the eruption.*

Microscopic Examination:—

(a) Gasserian ganglia.—In that portion of the right ganglion which receives the fibres of the inframaxillary division of the nerve, is an evident focal lesion destroying nerve-cells and nerve-fibres, over an area measuring 1·275 mm. by ·765 mm.

(b) Roots of 5th nerves central to ganglia.—In that segment of the right root in which we suppose the fibres that belong to the inframaxillary branch are distributed, scattered degenerated fibres are visible, and also three small fasciculi which are gravely affected, partly by a sclerotic process and partly by acute degeneration.

(c) Inframaxillary divisions of 5th nerves.—Scattered degenerated fibres are seen all over the section and also small sclerosed areas.

(d) Pons and medulla.—Definite acute degeneration of certain fibres of the sensory root of the 5th nerve of the right side, which can be traced down to the base of the substantia gelatinosa Rolandi, at the level of the 1st cervical anterior root.

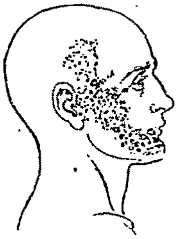

FIG. 18.

To show the distribution of the eruption in Case 18.

History.—There was insanity in his family. He was infected with syphilis at the age of 24, and for this he received no medical treatment other than that afforded by quacks. In May, 1895, he became melancholic after an attack of influenza, and was confined for two months in Cheadle Asylum.

State on admission.—Poorly nourished. Speech slurred and indistinct. Gait rather feeble and springy. Some facial tremor. Knee-jerks very brisk, equal; superficial reflexes present. Pupils of moderate size, hardly reacting at all to light; margins circular. Tongue protruded straight, but tremulous. Circulatory, respiratory, and alimentary systems normal. Urine: specific gravity 1020, no sugar or albumen. Mentally restless, excited, incoherent; memory defective.

Progress.—He gradually deteriorated mentally and physically, and eventually reached a condition of almost complete dementia; during his latter days he had several typical "general paralytic" seizures.

September 12, 1897.—A discrete crop of herpetic vesicles appeared on the chin and lower part of the cheek of the right side of the face; a few vesicles were also seen on the scalp a couple of inches above the ear on the same side. The skin intervening between these vesicles and also all the way up the lateral aspect of the cheek was markedly erythematous. The area affected corresponded to the cutaneous distribution of sensory fibres of the inframaxillary division of the 5th nerve.

September 21.—The vesicles had not increased in number, and those previously noted were now pustular. The erythema had persisted.

September 28.—The erythema was disappearing, and the vesicles were scabbing.

October 6.—Some seven or eight small scabbed patches were visible on the chin and three or four more similar patches on the scalp, a couple of inches above the ear. In the latter position there was also one pustule of considerable size.

October 12.—Death from "general paralytic" exhaustion thirty days after the first appearance of the herpetic eruption.

POST-MORTEM EXAMINATION.

Post-mortem examination thirty-four hours after death. Weather cold.

Body emaciated. Poor muscular and skeletal development. No localised muscle atrophy or contracture. Herpetic scabbing on chin and above ear on right side; skin otherwise healthy.

Calvaria normal.

Dura mater slack anteriorly; no abnormal thickening or unusual adhesions to bone or arachnoid. Dural sinuses partly filled with *post-mortem* clot. A moderate excess of clear, watery, sub-dural fluid; no free blood.

Pia-arachnoid markedly thickened and opaque universally; its removal caused patchy decortication.

Main arteries and veins healthy to the naked eye.

Cerebral hemispheres of fair size, equal; segments proportionally developed. Arrangement of convolutions simple; signs of general atrophy most marked frontally; sulci rather wide.

Cortex dark, fairly firm, hyperæmic, reduced in depth, with indistinct striation.

White matter appeared healthy.

Ventricles increased in size, contained an excess of fluid; ependyma faintly granular. Choroid plexuses congested.

Basal nuclei and other cerebral structures macroscopically normal.

Cerebellar cortex dark and thin.

Pons and medulla of normal size and shape, consistence fairly firm all through; gray substance generally hyperæmic; floor of 4th ventricle granular.

The pituitary body, cranial nerves, and Gasserian ganglia present no naked-eye alteration of any description.

An examination of the spinal cord was prohibited, but the three upper cervical segments were extracted through the foramen magnum.

Some old fibrous adhesions existed round the apices of both lungs. On section of the lungs general congestion and œdema was noticeable, and scattered throughout the lower lobes were firm patches of lobular pneumonia.

Heart small, muscle dark and firm; no valvular disease.

Aorta and large blood-vessels healthy.

Peritoneum normal.

Liver dark and firm. Gall bladder healthy.

Spleen normal. Kidneys dark and firm; capsule stripping cleanly.

Suprarenal glands, stomach, pancreas, small and large intestines, bladder, prostate gland, vesiculæ seminales and testes free from morbid change. No obvious syphilitic scarring could be found on the penis.

MICROSCOPIC EXAMINATION.

A microscopic examination was made—(*a*) of both Gasserian ganglia, (*b*) both 5th nerve-roots in their extrapontine course, (*c*) both inframaxillary nerves, (*d*) the crus cerebri, pons varolii, and medulla oblongata.

(*a*) *Gasserian Ganglia.*

Method of examination.—The ganglia were primarily hardened in a mixture of equal parts of formalin 4 per cent. and Müller's fluid, afterwards in absolute alcohol, embedded side by side in celloidin, and cut transversely together on one and the same block. In this manner in every section we obtained a view of both ganglia, and we were enabled with ease and convenience to compare the healthy and affected sides. The sections were kept in strict serial order, and every alternate one was stained by the old copper-hæmatoxylin method of Weigert and mounted. In all 110 sections were examined (plate 9.)

In the first sections, along the dorsal margin of the right ganglion, at about the junction of the outer with the middle 3rd, situated immediately below the dura and almost opposite the motor root, are three small nerve-bundles which are obviously diseased; the principal change in them must be described as a sort of sclerosis, that is to say, they stain very much more palely than adjoining bundles, are to a large extent deprived of nerve-fibres, and some of those fibres which remain appear to be swollen; furthermore, these bundles contain an excess of connective tissue.

These three bundles can be readily followed along section by section, gradually assuming a more external position, until in the thirty-first section they split up to form five smaller fasciculi.

The corresponding nerve-bundles in the left ganglion are free from obvious change, and so likewise are all the other nerve-bundles motor and sensory, all the ganglionic substance, and the pia-arachnoid and dura cut in the first thirty-eight sections.

At about the thirty-ninth section signs of thickening and excessive development of the pia-arachnoid overlying the above-mentioned sclerosed bundles of the right side becomes evident. In the succeeding sections the bundles approach, and in the forty-sixth section join, a portion of ganglion pertaining to the inframaxillary division of the nerve. This portion of the ganglion is infiltrated by numbers of small round cells, and in the forty-ninth section it becomes converted into a definite focal lesion, which gradually increases in dimensions to attain its maximum size at about the fifty-third section; it then tails off again and disappears in the fifty-eight section.

Described in detail where it is best developed the lesion has the following character:—It is situated in a tongue-shaped portion of the ganglion on the dorsal aspect, immediately beneath the dura mater, at the junction of the middle with the outer one-third of the ganglion; directly opposite to it, on the ventral surface, lies the motor root of the 5th nerve. In form, on transverse section, the focus is roughly oval, its greatest transverse diameter being 1·275 mm., its greatest vertical ·765 mm. Structurally it is made up of a large central nucleus, which is tinted brown, but is for the greater part of indefinite composition. In it can be seen some scattered small round cells, a few engorged blood-vessels, and interspersed here and there what appear to be the remnants of nerve-cells. Encircling the central position is a thin purple-stained zone in which small round cells are abundantly congregated. Enveloping this zone, extending up to the pia on the free surface and for some distance into the surrounding ganglionic substance, is a wider zone, which is extremely densely infiltrated with small round cells and in which remains only of nerve-cells and nerve-fibres can be seen along with congested blood-vessels. Outside this zone the nerve-cells and fibres of the ganglion soon assume a healthy aspect. The pia covering the mass is thickened and infiltrated with small round cells. The inner surface of the over-lying dura is also slightly affected in a similar manner. The remainder of the ganglionic substance and the other bundles of nerve-fibres of this ganglion are healthy.

Sections fifty-nine to sixty-five show a gradual diminution in the over-cellularity of the ganglionic tissues before occupied by the focus, and there now appears, on the outer side of this area, a fasciculus of nerve-fibres of considerable size, of which about one-third in sectional area is sclerosed. This bundle can be followed into the peripheral trunk of the inframaxillary division and disappears from view at about the seventy-fifth section.

The remaining sections exhibit no change of importance.

The left Gasserian ganglion is free from any signs of disease

(*b*) *Roots of 5th Nerves Central to Ganglia.*

Method of examination.—Both roots (right and left) were stained by the method of Marchi, fixed together in juxtaposition in one block in celloidin and cut serially in the transverse direction; every alternate section of the series was mounted.

Commencing with the sections of the more peripheral portions of the root, the right can always be distinguished from the left by the existence of degeneration in it. This degeneration is not of a striking character, but it is, nevertheless, just what one would expect when one takes into consideration the comparatively slight extent of the herpetic eruption. It is principally confined to three small fasciculi lying at the periphery of the section, opposite to the motor root, which root can always be identified in being uniformly composed of fibres of large calibre, whereas the sensory bundles contain fibres of mixed calibre, large and small. The change which these three bundles present is chiefly of a sclerotic character and is suggestive of an acute parenchymatous degeneration some weeks old, of which the blackened fatty masses have been to a great extent absorbed; thus the ground of the affected fields is white in colour and scattered over it are round or irregular-shaped black masses and an appreciable number of empty, swollen, primitive sheaths. In this way about three-fourths of one bundle is affected, about one-half the next and about one-third of the next. Taken altogether it cannot be said that more than one-twentieth part of the sensory root is so involved.

In addition to the sclerotic affection of these three bundles, all the other bundles in that segment of the root which one regards as being composed of inframaxillary branches show blackened degenerated fibres disseminated throughout them.

The other bundles, which are probably derived from the 1st and 2nd branches of the nerve, and also the motor root, are quite free from disease.

The root of the left side is absolutely healthy and shows nothing resembling that on the right side.

The changes in the right root above noted can be plainly traced centrally on to the point of entry of the root into the side of the pons varolii.

Peripherally they evidently correspond with the three fasciculi noted as being sclerosed in the early sections of the right ganglion.

(*c*) *Peripheral Nerve-trunk of Inframaxillary division.*

The sclerotic condition of a bundle of nerve-fibres leading away from the focal lesion in the right ganglion into the nerve-trunk has already been alluded to. Sections of this trunk a short distance peripheral to the ganglion, stained by the method of Marchi, show a considerable number of acutely degenerated fibres scattered fairly evenly over the various bundles comprising the trunk, and likewise a partial sclerosis of some bundles. The perineurium is unchanged.

The facial branches of the nerve could not be examined.

(*d*) *Pons Varolii, Crus Cerebri and Medulla Oblongata.*

Method of examination.—To study the condition of the 5th roots in their intrapontine and intramedullary course, the crus cerebri, pons and medulla were cut up transversely into thin slices and stained by the method of Marchi.

In the first place the motor, so-called descending or cerebral root, is quite free from degeneration from its point of issue from the pons to as far up in the crus cerebri as it is possible to trace it.

It might also be mentioned here that in the sections above the level of entry of the 5th roots, the various systems of nerve-fibres, viz., the superior cerebellar peduncles, the lemnisci, the posterior longitudinal bundles, the fibres of the tegmentum, the transverse pontine fibres, &c., show no degeneration whatever, but in the motor or pyramidal tracts of either side disseminated acutely degenerated fibres may be recognised. This degeneration is, no doubt, part of the "general paralysis," and is unconnected with the herpetic lesion.

The sensory, so-called ascending or spinal root of the right side shows marked degenerative changes in its entire course. Described in detail these are as follows (plate 13):—

(*a*) Sections which catch the right trigeminal root just at its point of entry into the pons show disseminated degenerated fibres in all the bundles of the sensory root, but in the outer portion of the root two or three fasciculi are observed which are gravely affected and contain numerous rows of blackened fatty masses, indicating acute degeneration. These are probably the same bundles as were described as being partially acutely degenerated and partially sclerosed in transverse sections of the root between the pons and the ganglion.

(*b*) Sections slightly more caudalwards show similar degeneration in the intrapontine part of the sensory root, obliquely cut as it courses upwards and inwards in the direction of the trigeminal nucleus.

(*c*) The next sections show strands of degenerated fibres quite close up to the sensory trigeminal nucleus, and also among the cells of the nucleus a few degenerated fibres of small calibre can be seen running. The method is not adapted for the display of changes in the nerve-cells themselves. The motor nucleus is clearly visible and there is no fibre degeneration in it.

Without serial transverse or longitudinal sections it is impossible to see the exact relation of the degenerate sensory fibres to the sensory nucleus, but the majority of the fibres, at any rate, do not seem to come into connection with the nucleus, but appear to curve abruptly downwards and ventral to it.

(*d*) In sections slightly below the level of the 5th nucleus the sensory root is seen forming up into a pear-shaped area with the thin end upwards. Scattered over the upper two-thirds of this area many degenerated fibres are seen, some cut transversely but the majority obliquely. In the lower one-third a few diseased fibres only are to be found.

No degenerated fibres are anywhere seen running beneath the floor of the 4th ventricle to cross to the opposite side.

(*e*) Sections opposite the 6th nuclei are similar to the last.

(*f*) In sections opposite the 7th and 8th roots the degenerated fibres in the right sensory root are all cut more or less transversely; they are scarce in the lower one-third of the field, moderately numerous in the upper third and most numerous at about its middle.

The roots of the 7th and 8th nerves are intact.

(*g*) Sections opposite the 9th and 10th roots show similar degeneration.

(*h*) Opposite the great olive, where the root approaches the surface, it is to be noted that the degenerated fibres are not so numerous as they were above, and it is again to be observed that the lower one-third of the field contains few diseased fibres.

(*i*) Opposite the main decussation of the fillet degenerated fibres are seen scattered throughout that part of the 5th root which lies between the dorsal half of the substantia gelatinosa Rolandi and the surface adjoining the funiculus cuneatus, and degenerated fibres are seen running in the most dorsal part of the substantia gelatinosa. In the more ventrally situated part of the same field degenerated fibres are scarce.

(*j*) Opposite the upper part of the pyramidal decussation, the distribution of degenerated fibres in the right 5th root is similar, but they are becoming markedly scarcer. Other degenerated fibres are seen in the innermost dorsal part of the base of the substantia gelatinosa, not far removed from the glosso-pharyngeal root.

(*k*) Opposite the remainder of the pyramidal decussation and opposite the 1st cervical root the degeneration is indistinct, but at the base of the substantia gelatinosa, in its most dorsal part, is an obvious collection of small black dots, which is not represented on the opposite side.

Below this level degeneration cannot be definitely traced.

There remains to be mentioned that in all the above sections scattered degenerated fibres of large calibre were found throughout the pyramidal tracts of both sides; as already stated, this degeneration is to be associated with the general paralysis which caused the patient's death.

Likewise in the posterior longitudinal bundles and lemnisci of both sides are a few degenerated fibres (about half a dozen). These may be attributed to the same cause as the pyramidal degeneration.

The sensory root of the 5th nerve of the left side examined throughout shows nothing at all resembling the condition seen in the right root.

No other cranial nerves issuing from or entering the pons or medulla show degeneration.

Case 19.—William C., aged 43 (Rainhill Asylum). Admitted September 25, 1895. Died May 8, 1896.

SUMMARY.

On November 1, 1895, *an herpetic eruption appeared on the forehead immediately above the right eyebrow* (*fig.* 19). *Death from general paralysis, May* 8, 1896, 190 *days after the appearance of the eruption.*

Microscopic Examination :—

There seems to be a focus of disease in the ganglionic substance pertaining to the ophthalmic division of the right 5th nerve, but as there was a fault in the method of examination we prefer to withhold any definite statement concerning this lesion.

In the root of the right 5th nerve central to the ganglion and in that part of the root which we take to be a portion of the ophthalmic division, several small nerve-bundles are seen which are partially sclerosed, but in the roots of the nerves within the pons and medulla no difference between the two sides can be appreciated.

There is no noteworthy alteration in the ophthalmic division of the nerve peripheral to the ganglion.

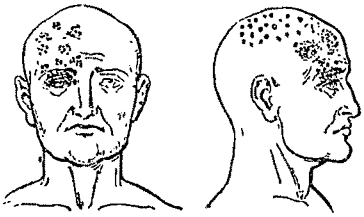

FIG. 19.

To show the distribution of the eruption in Case 19.

History.—He was married and had had one child only, which was still-born. Syphilis was not denied. He was an egg merchant, and drink and failure in business were assigned as the causes of his insanity.

On admission.—He was a weak and feeble general paralytic. Speech blurred and indistinct. He could walk, but was distinctly ataxic. Muscular and well nourished. No actual paralysis.

Knee-jerks absent. Pupils equal and did not react to light. No paralysis of the face. Tongue tremulous and somewhat wasted. Circulatory and respiratory systems normal. Urine normal when collected by catheter.

Mentally he had grandiose delusions, was restless and resistive, and wet and dirty in his habits.

November 1, 1895.—He developed herpes of the forehead, which reached its full development two days later (fig. 19). The cornea remained unaffected throughout, and the disc and fundus were normal.

May 8, 1896.—He was seized with convulsions, from which he never recovered, dying 190 days after the first onset of the herpetic eruption.

POST-MORTEM EXAMINATION.

An examination of the head only was allowed; this was made seventeen hours after death.

State of nutrition fair. A large patch of skin on the front and to the left side of the chin was white and cicatricial, and here there was no growth of beard; this was the result of a burn. On the forehead, immediately above the right eyebrow, was a small and indistinct patch of herpetic pigmentation. Had it not been known that the patient had previously suffered from herpes in that position, this would probably have escaped observation.

Scalp and cranium normal.

Weight of encephalon 1,255 grammes. Dura mater relaxed anteriorly; no abnormal adhesions or thickening. Dural sinuses filled with black blood clot. Main arteries looked rather tough and white, but were not calcareous.

Cerebro-spinal fluid of clear watery character, markedly in excess. No subdural membrane or blood.

The arachnoid generally presented the blue milky opacity so commonly seen in general paralysis.

The pia mater was considerably thickened, difficult to remove, and hyperæmic; on stripping it decortication occurred in the frontal and parietal regions.

The cerebral hemispheres were equal in size, and the individual segments showed a normal development; but there were indications of general atrophy, most marked in the frontal region. The sulci were wide and shallow.

The right hemisphere unstripped weighed 540 grammes, the left 542.

Cortex dark, somewhat soft, hyperæmic, thin, and indistinctly striated.

No obvious change in white matter. General consistence rather soft.

The lateral ventricles were markedly dilated, and contained an excess of fluid. The ependyma over the basal nuclei was granular.

The basal nuclei were of dark colour and rather small.

The cerebellum weighed 127 grammes. Cortex dark and thin. General consistence rather soft. No lesions.

Pons and medulla together weighed 29 grammes. Gray substance dark in colour. Ependyma of 4th ventricle thick and granular.

Pituitary body and cranial nerve-roots presented no macroscopic morbid change.

The Gasserian ganglia and the portions of the three divisions of the 5th nerves, which were carefully extracted for detailed examination, showed no abnormality to the naked eye.

Microscopic Examination.

A microscopic examination was made of—(*a*) the Gasserian ganglia of both sides, (*b*) the 5th roots of both sides, (*c*) the ophthalmic divisions of the 5th nerves of both sides, (*d*) the crus, pons varolii, medulla oblongata, and the upper part of the spinal cord.

(*a*) *Gasserian Ganglia.*

Method of examination.—Each ganglion was divided transversely into two halves, and after staining by the method of Marchi, the distal portion was cut longitudinally and the central portion transversely.

It might here be noted that this was one of the earliest cases of herpes which we had the opportunity of submitting to microscopic examination; and experience has since taught us that the method of examination that we adopted was a faulty one. At that time our method aimed principally at the discovery of acute degeneration of nerve-fibres, and we were not alive to the importance of searching the ganglion mass closely for a local lesion, else the ganglion would not have been divided in the manner above described; for, as the description indicates, by so doing the lesion was probably obscured.

Right ganglion.—Taking first the transverse sections. These show a portion of the ganglionic substance pertaining to the ophthalmic division of the nerve along with the roots of the superior and inferior maxillary branches and the motor root. In none of these is there any acute degeneration, but on the ventral side of the section, not far to the left of the motor root and in close apposition to the ganglionic substance of the ophthalmic division of the nerve, there is one small bundle which presents an unhealthy appearance; it is deprived of a certain number of fibres, it contains indefinite débris, and its blood-vessels are dilated. Furthermore, in other sections this bundle can be seen making in the direction of the ganglionic substance of the ophthalmic division.

Examining next the longitudinal sections, it is seen that those portions of the ganglion pertaining to the superior and inferior maxillary branches look healthy; but in several sections a portion of the ganglionic substance into which the ophthalmic branch runs has the appearance of being diseased. At one spot there seems to be the remains of a hæmorrhage, indicated by a collection of red blood corpuscles and a local destruction of nerve-cells; but unfortunately this portion lies just at the margin of the line of section by which the ganglion was divided into two halves, and it is therefore impossible to say certainly that this represents a hæmorrhage.

Left Gasserian ganglion.—The ganglion of the left side exhibits no change similar to that above described.

Fifth Nerve-roots.

Right.—Stained by the method of Marchi.

In the sections of the right root there are several small bundles which have a partially sclerosed aspect, but do not show acute degeneration; these are situated in that part of the root furthest removed from the motor root.

Left.—Normal.

Ophthalmic Branch of the 5th Nerve.

Stained by the method of Marchi.

From both right and left sides portions of the trunk before division, and portions of the frontal branch, showed no positive change.

Crus Cerebri, Pons Varolii, Medulla Oblongata, and Spinal Cord.

The crus, pons, and medulla were cut up transversely into thin slices and stained by the method of Marchi, and portions of the cervical cord were treated in the same way.

The sections of the crus and those of the pons above the level of entry of the 5th nerves show that the cerebral root of the 5th nerve is normal; there is likewise no degeneration in any of the other of the nerve tracts found at these levels, excepting the pyramidal tracts, and in these on either side acutely degenerated fibres of large calibre are disseminated. This degeneration is to be referred to the general paralysis from which the patient suffered, and it is visible not only here, but also in the sections from all the other levels examined.

In the sections which show the 5th roots immediately after their entry into the pons, the appearances are disappointing and no pronounced degeneration is visible on either side.

Similarly in the sections which display the course of the sensory root of the nerves, there is not sufficient change in the roots of the two sides to enable us to declare that the right is diseased and the left healthy.

A certain number of fibres in the roots of the 8th nerves of both sides show what we take to be true degeneration, but the

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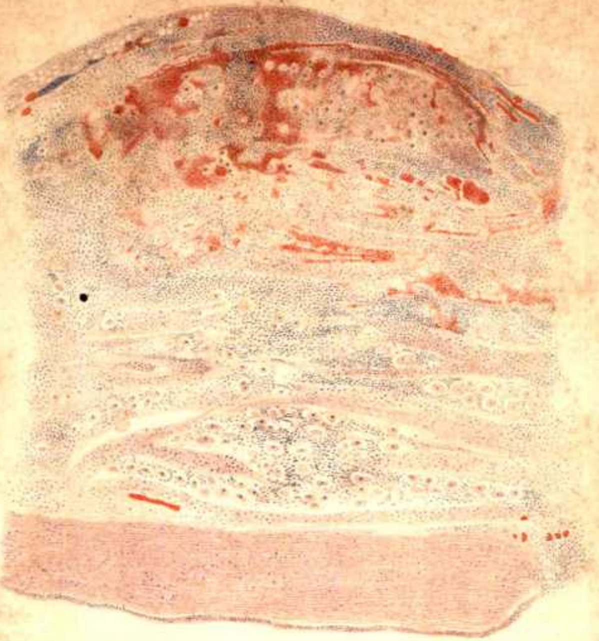

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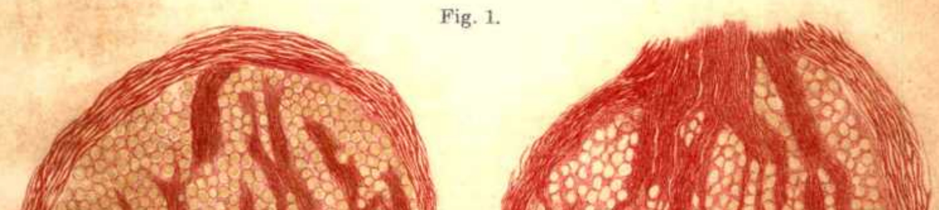

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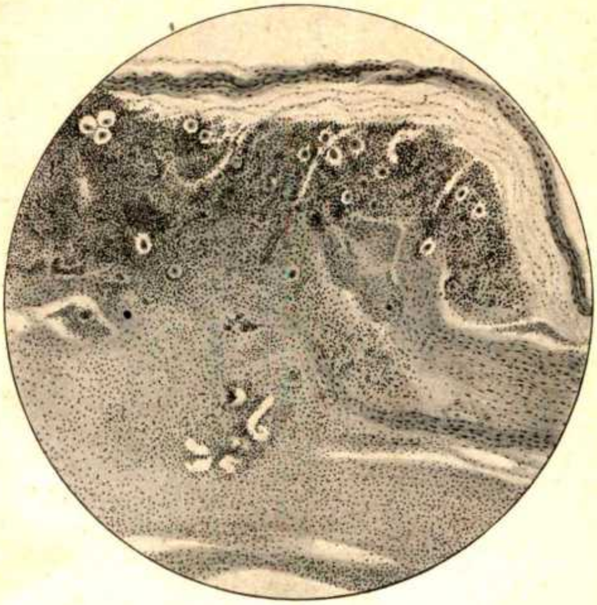

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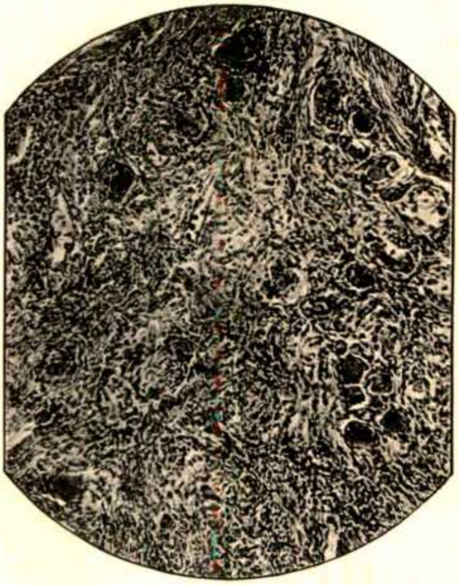
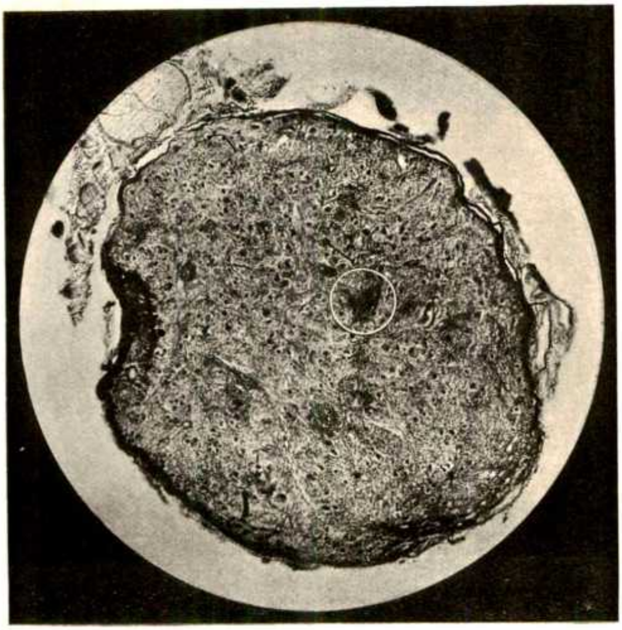


FIG. 2.

BRAIN 1

PLATE 3.



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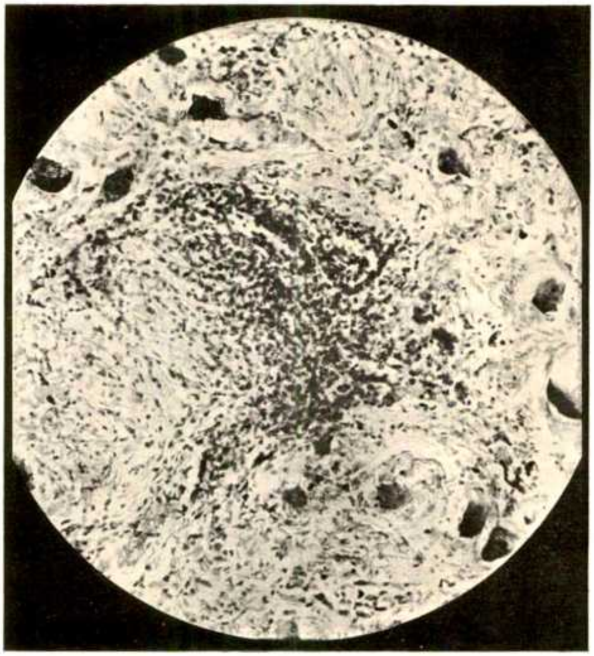

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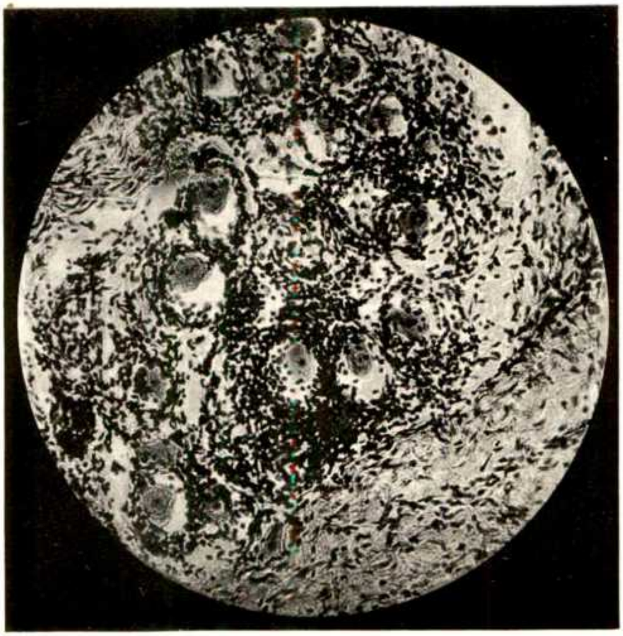

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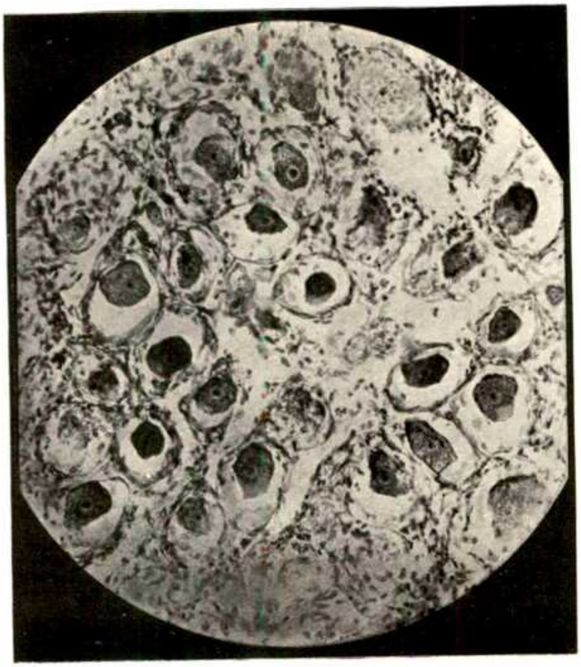

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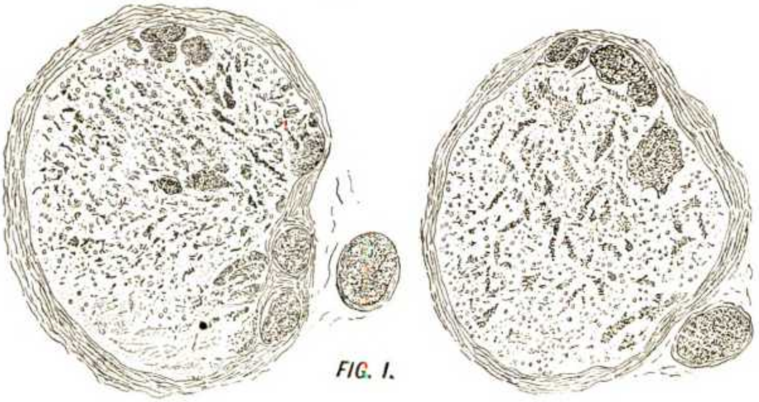

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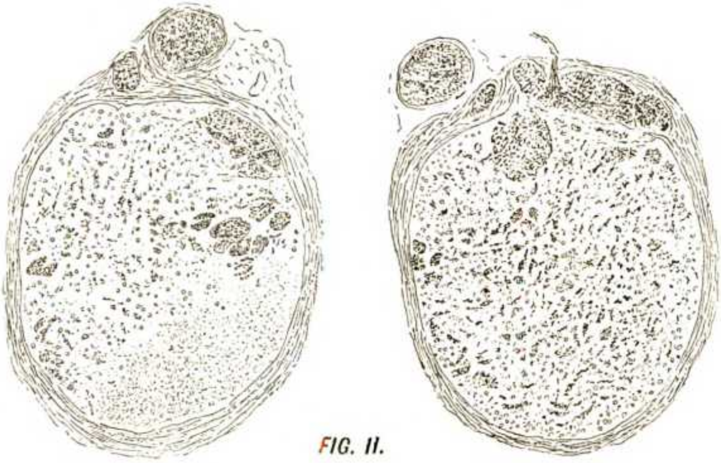

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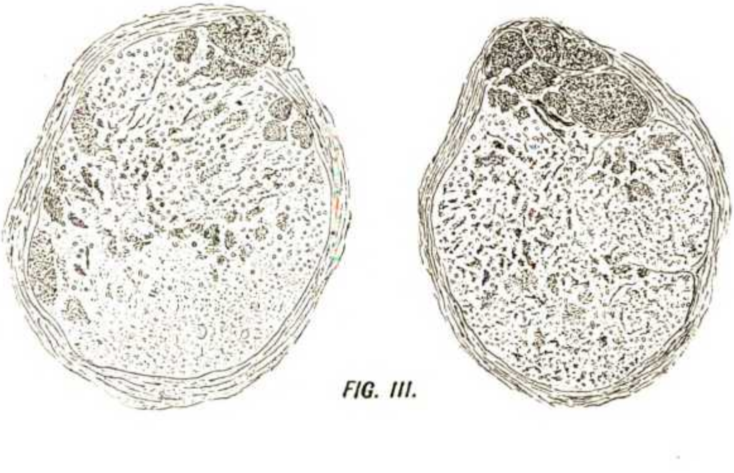
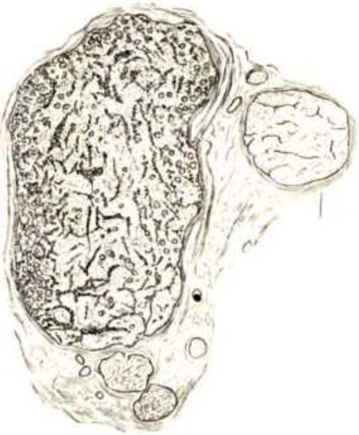


FIG. III.

PLATE 6.



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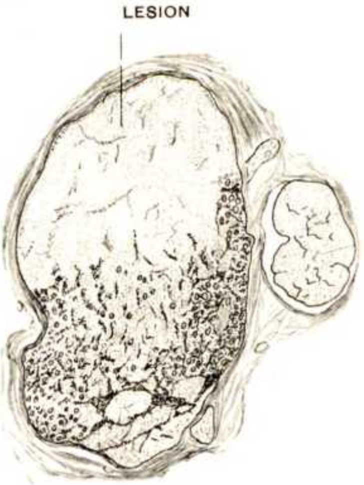

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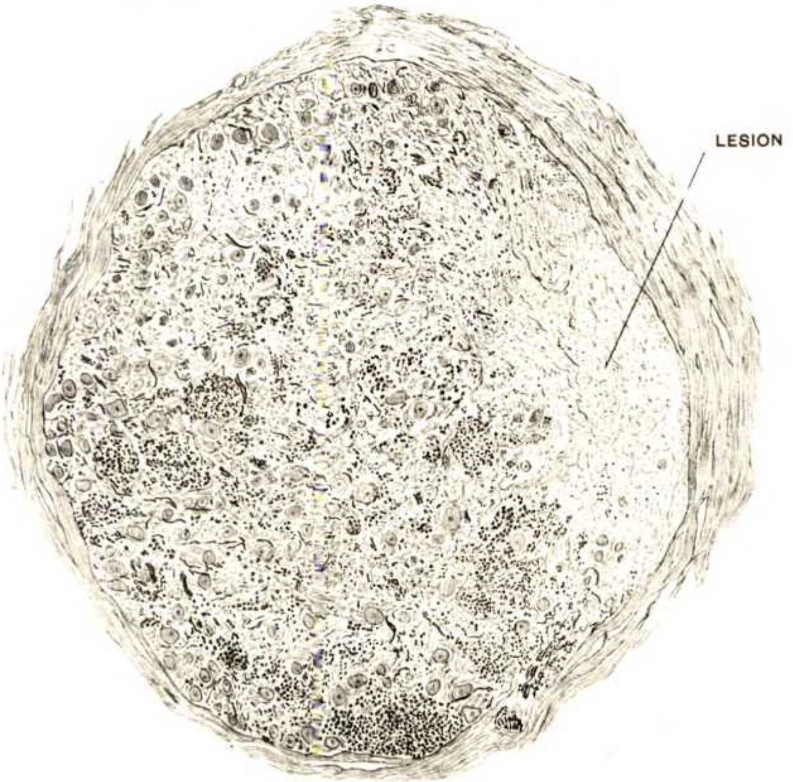

FIG. 2.

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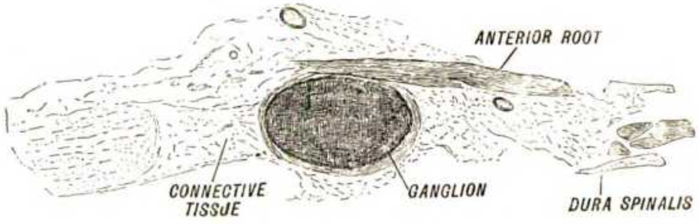

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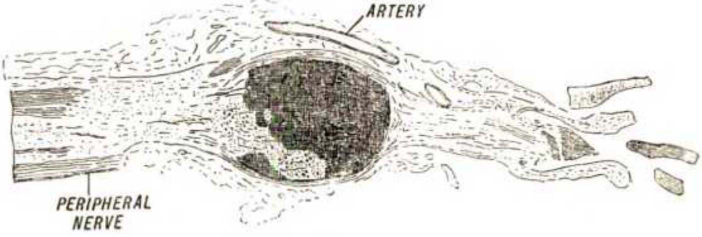

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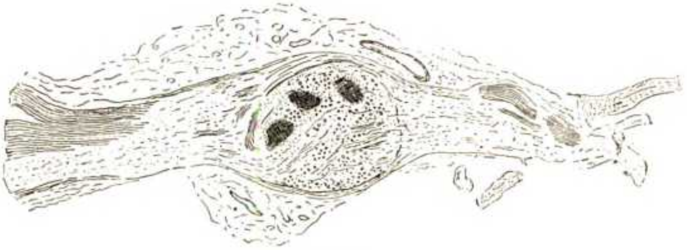

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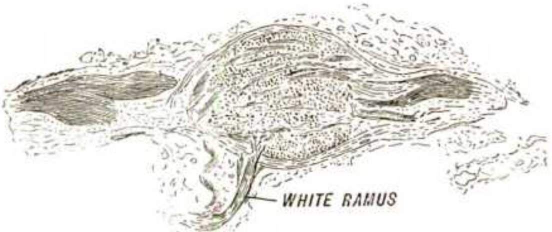
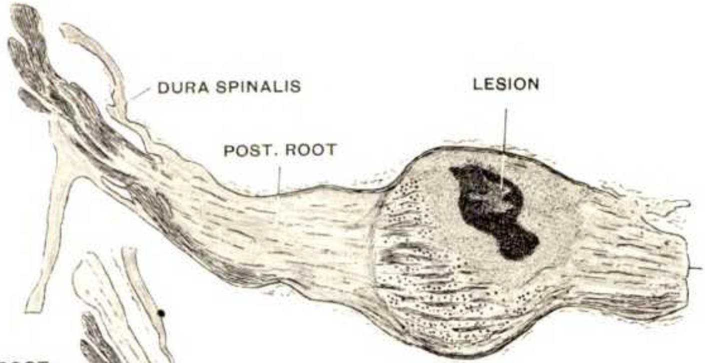


FIGURE IV.

PLATE 8.



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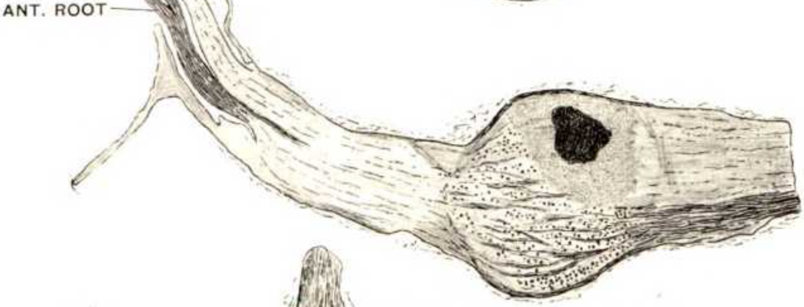

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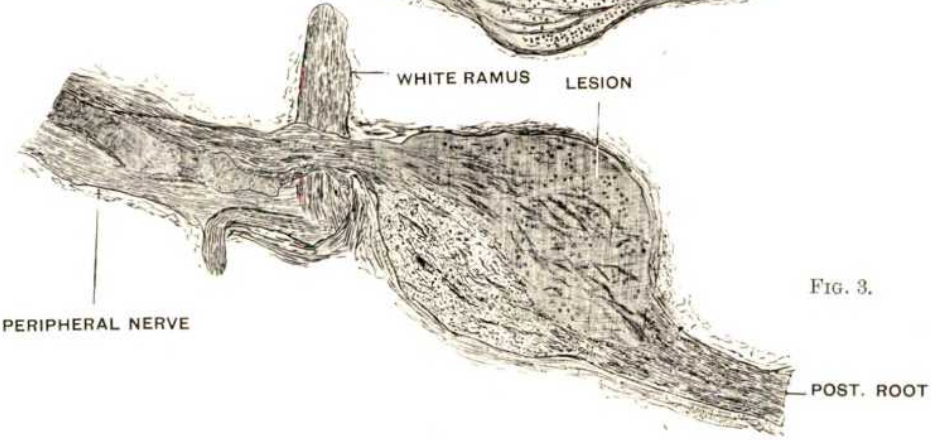

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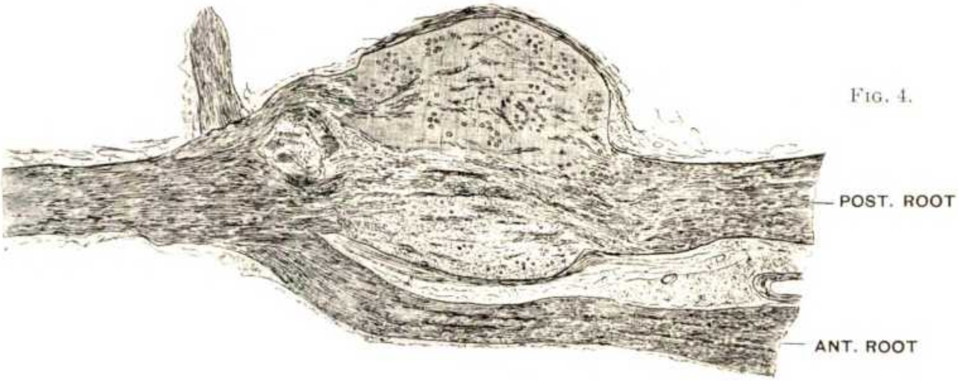
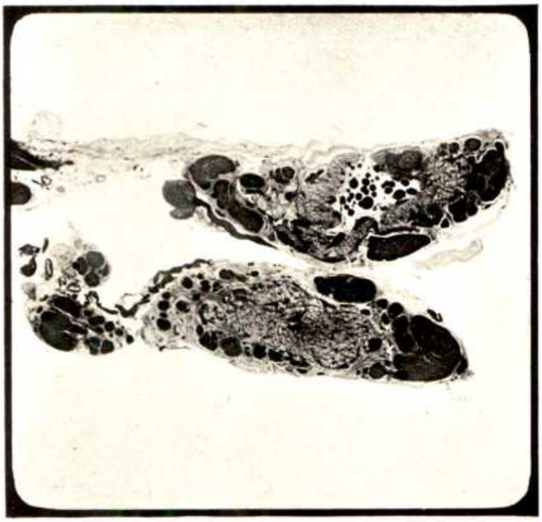
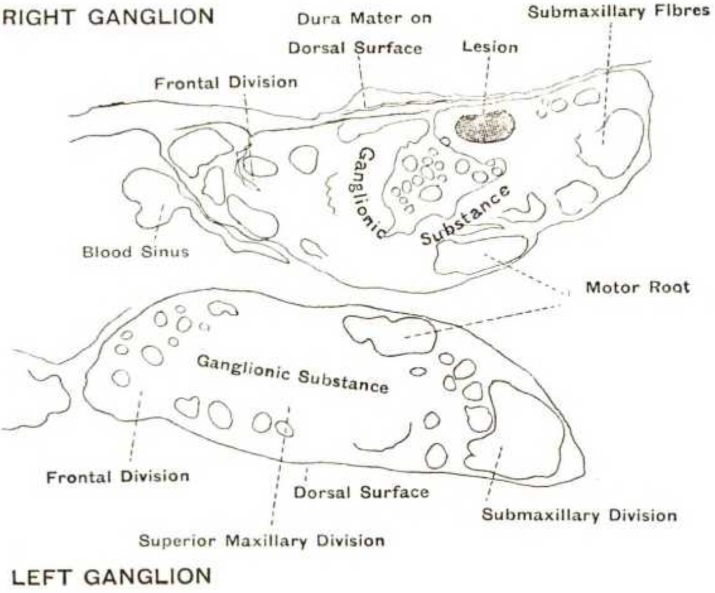


FIG. 4.

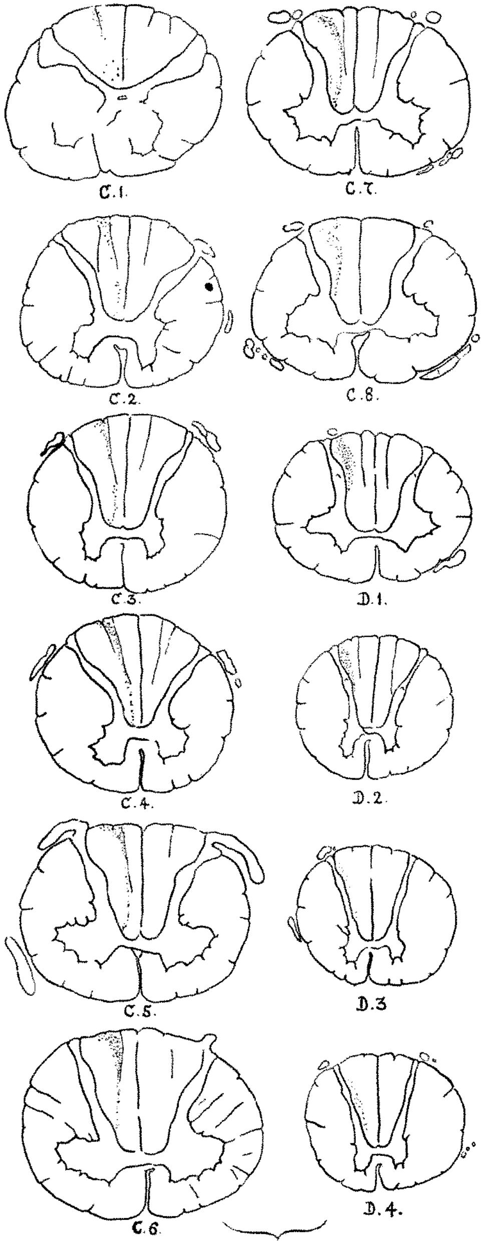
PLATE 9.





KEY TO PHOTO OF GASSERIAN GANGLIA.

PLATE 10.



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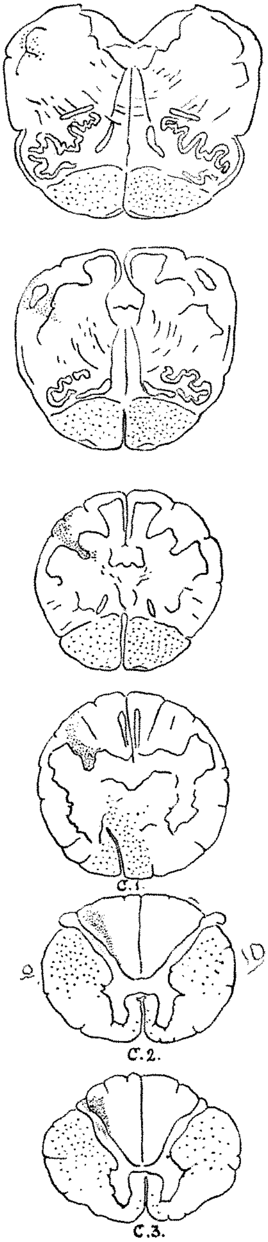
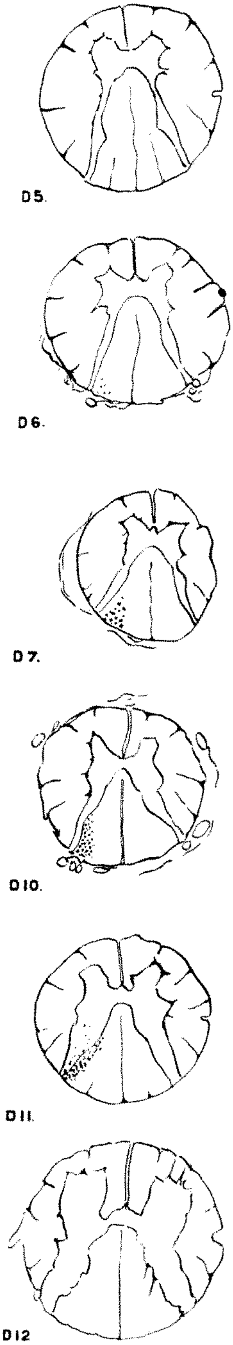


FIG. 2

PLATE 11



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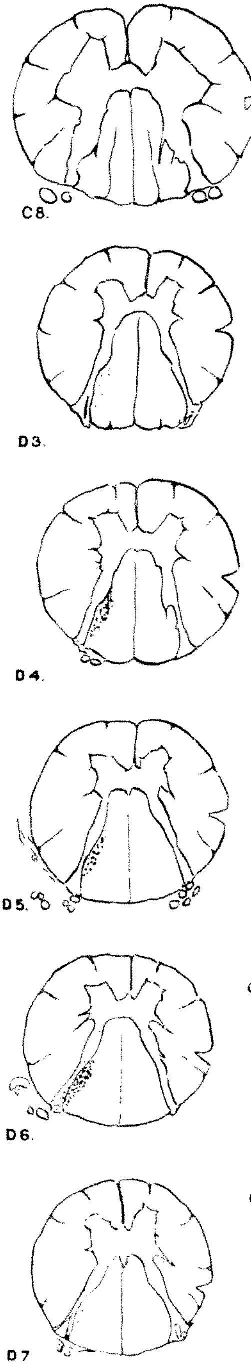

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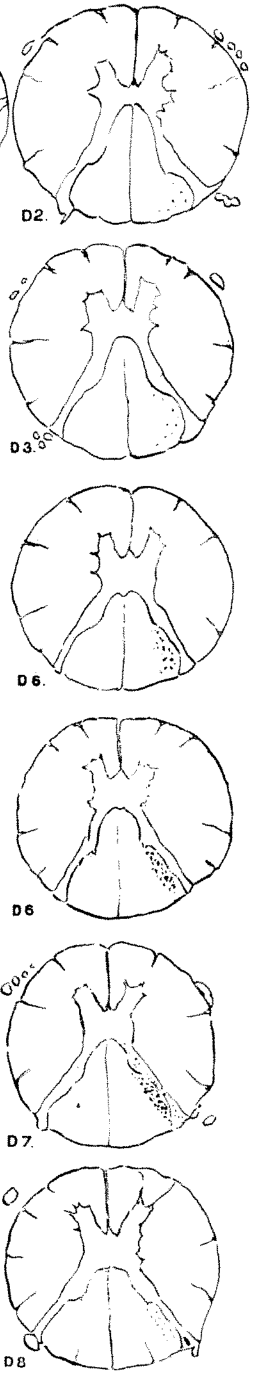
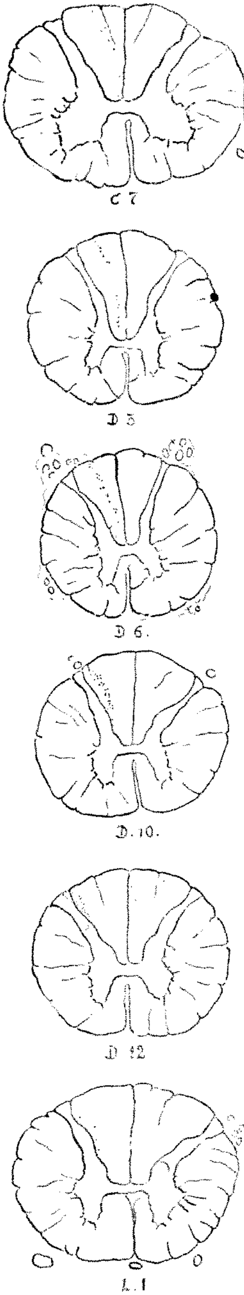


Fig. 3.

Brain 2 a

PLATE 12.



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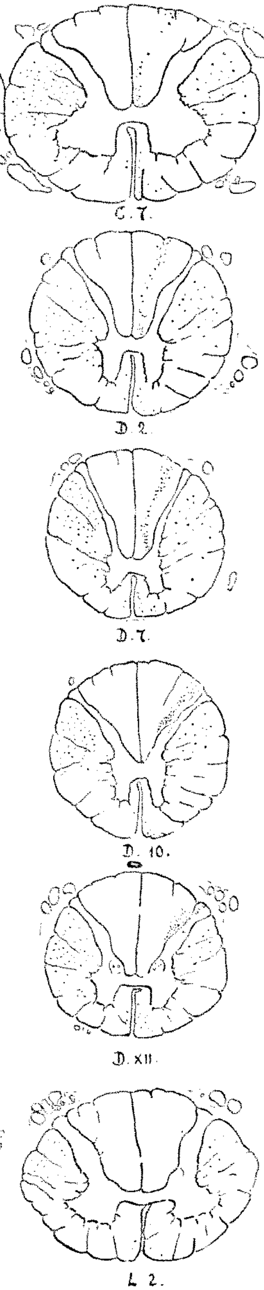

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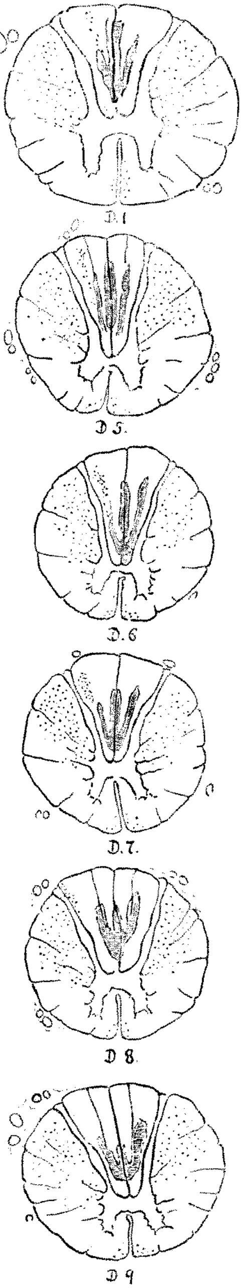

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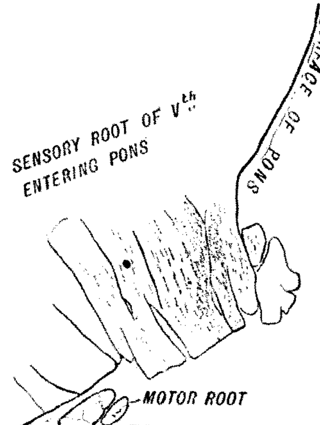
PLATE 13.



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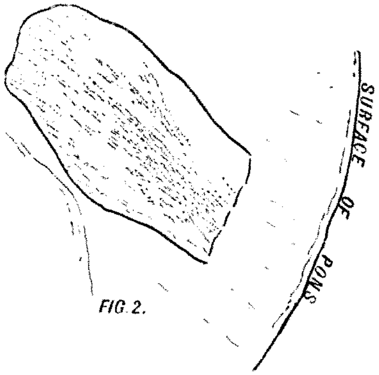

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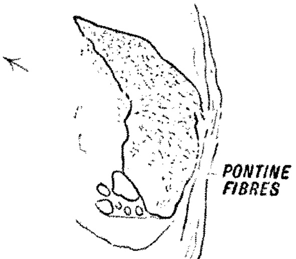

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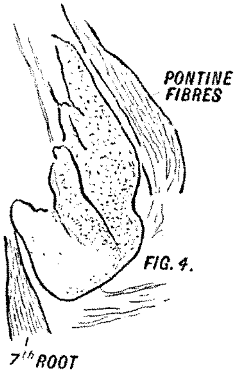

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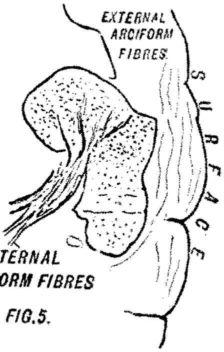

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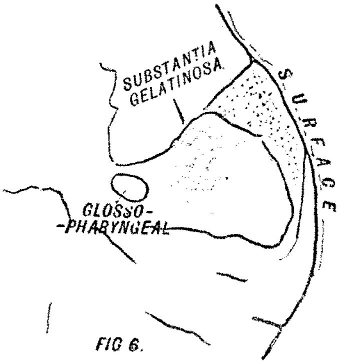
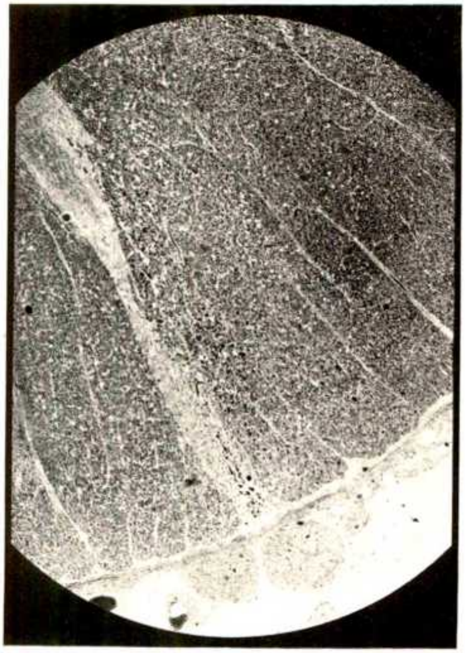


FIG. 6.

PLATE 14.



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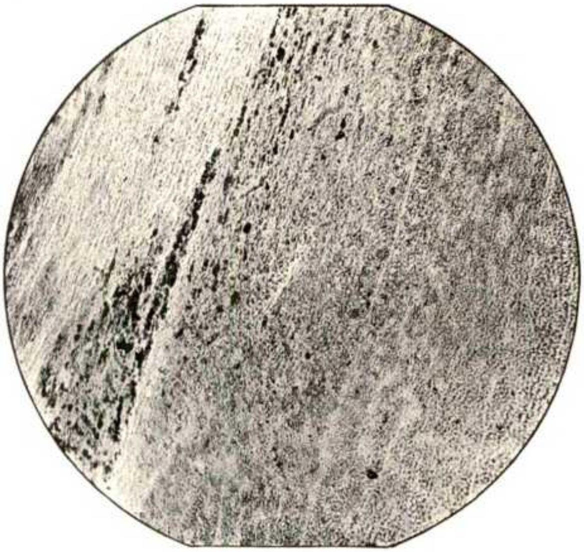

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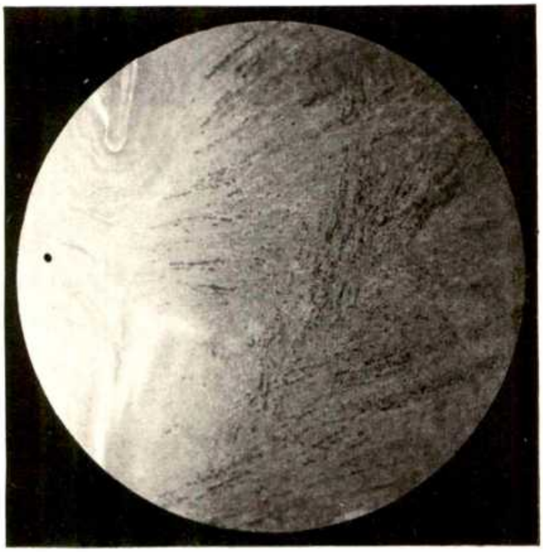

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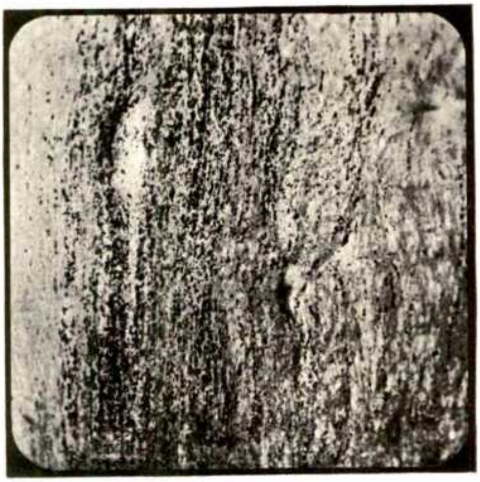

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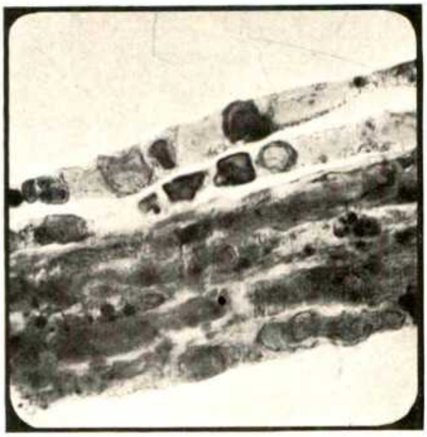
PLATE 16.



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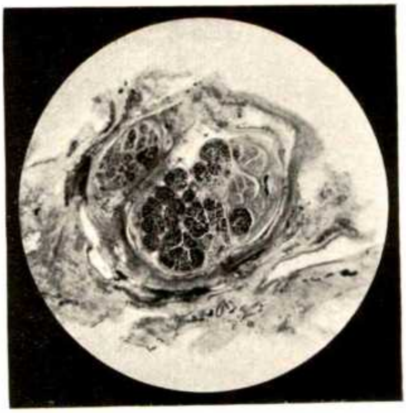

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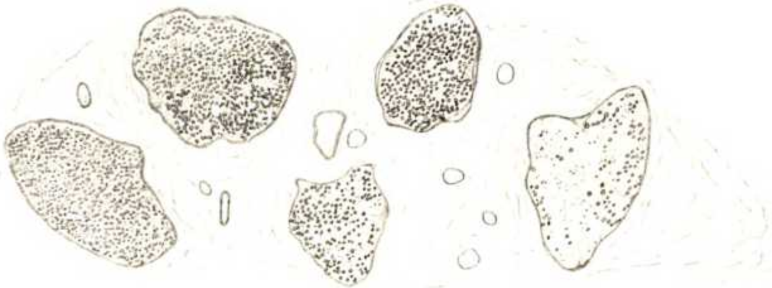

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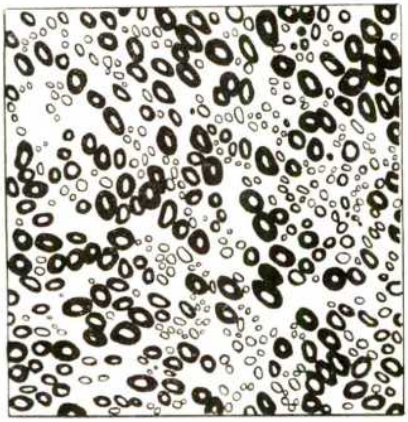

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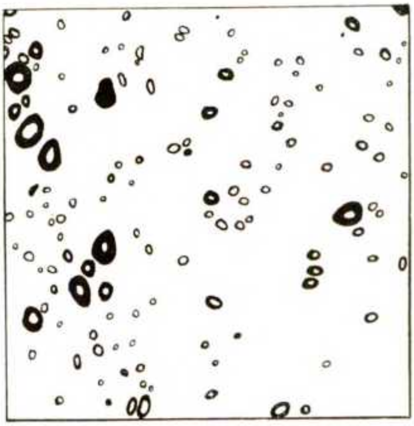

FIG. 5.

corresponding nuclei are healthy, and the significance of the change is doubtful.

In the remainder of the medulla and in the upper part of the spinal cord there is no change referable to the herpes.

Case 20.—John A., aged 38. Admitted to Claybury Asylum September 27, 1898. Died March 13, 1899.

SUMMARY.

A case of dementia paralytica, who suffered from a slight attack of herpes zoster over the 10*th dorsal area* (*fig.* 20) 139 *days before his death from broncho-pneumonia.*

No scars were seen on the body at death, and an examination of the nervous system failed to reveal any lesions corresponding in any way with the herpes zoster.

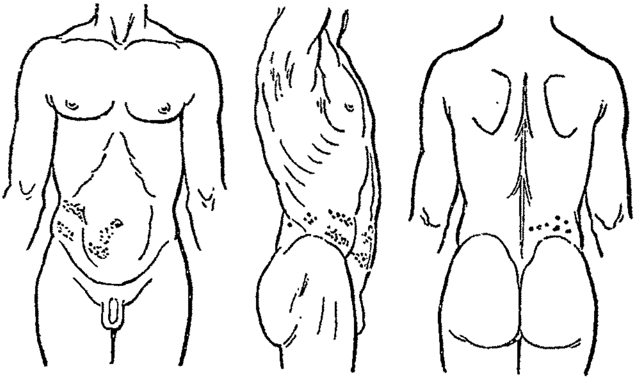

FIG. 20.

To show the distribution of the eruption in Case 20.

He was so grossly demented on admission that no trustworthy history could be obtained.

He was a fat, well-nourished general paralytic, with slow, slurred speech. Had delusions of grandeur and was rambling and incoherent in conversation. His pupils reacted to accommodation but not to light. Knee-jerks exaggerated.

By the end of October he was wet and dirty, sitting all day by himself. His speech had become much more hesitating.

On October 25 an eruption of herpes zoster appeared over the 10th dorsal area (fig. 20). In front the eruption was fairly profuse but behind was poorly marked. It was not a severe outburst.

By February, 1899, he was confined to bed entirely, and he died on March 13 of hypostatic pneumonia, 139 days after the appearance of herpes zoster.

POST-MORTEM EXAMINATION.

Twenty-four hours after death. The body had been kept in the cold chamber at a temperature just below freezing-point.

Post-mortem rigidity was not present. Nutrition of body fair.

Brain.—In the subdural space in the left posterior and middle fossæ was a thin, organised, rusty membrane, the earliest form of pachymeningitis hæmorrhagica. The pia over the frontal and parietal lobes was markedly thickened and opaque. Over the temporal and occipital lobes some thickening was seen but it was less marked. Gelatinous exudation was present in the subdural space.

The brain was moderately wasted, the right hemisphere weighing 563 grammes, the left 560 grammes. There was slight general wasting of the frontal and parietal convolutions. Striæ of the cortex invisible. Puncta vasculosa well marked. Both ventricles were slightly dilated, granular, and filled with clear fluid.

The cerebellum was normal.

The fourth ventricle was granular.

Thorax.—The right lung was in an advanced stage of broncho-pneumonia throughout and presented many areas of collapse. The upper lobe was in a more advanced stage of disease than the lower. The bronchi were full of semi-purulent mucus.

The upper and lower lobes of the left lung were adherent to the chest wall by recent adhesions, and the posterior surface was covered with a thin layer of organised lymph. The upper lobe was in an advanced condition of broncho-pneumonia. The lower lobe showed the same change in a less advanced form.

The heart was normal except for slight thickening and puckering of the mitral valve.

The aorta showed the first stage of atheroma.

Abdomen.—Liver congested but otherwise normal.

Kidneys normal.

Spleen normal.

MICROSCOPICAL EXAMINATION.

(*a*) *Posterior Root Ganglia.*

The 8th, 9th, 10th, 11th and 12th dorsal ganglia were hardened in 96 per cent. alcohol, embedded in paraffin and cut in series. They were stained by Nissl's methylene blue method and counterstained with safranin or eosin.

In no case could we find any gross abnormality in the capsule, cells, or interstitial tissue of any of these ganglia.

(*b*) *Posterior Nerve-roots.*

The 9th, 10th, 11th and 12th posterior nerve-roots on both were hardened in Müller's fluid and stained by Marchi's method. The stain succeeded admirably, but no root showed any degeneration.

(*c*) *Spinal Cord.*

Every segment of the spinal cord was stained by Marchi's method and by Schäfer's modification of the Pal method (Marchi-Pal).

The cord showed well-marked Marchi degeneration in both the direct and crossed pyramidal tracts on both sides. This acute degeneration appeared to be accompanied in the dorsal region by slight and doubtful sclerotic changes.

The posterior columns and root zones were everywhere absolutely normal.

(*d*) *Cortex.*

Portions of the cortex from the ascending parietal and Broca's convolutions on the right and left sides showed thickened membranes, dilated vessels and marked absence of the tangential fibres.

Case 21.—William C., aged 49. Admitted to Claybury Asylum November 26, 1895. Died March 14, 1897.

SUMMARY.

On admission showed marked dementia paralytica. Towards the end of the summer of 1896 *he developed a crop of herpes zoster over the area in fig.* 21. *He died about eight months after the eruption. No change could be found corresponding to the herpetic eruption.*

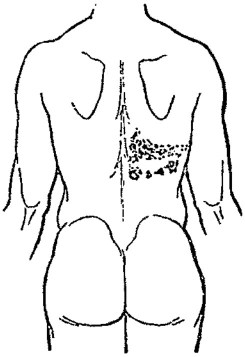

FIG. 21.

To show the distribution of the eruption in Case 21.

No history of any importance could be obtained.

On admission.—He was suffering from marked dementia, and his memory was much impaired. His speech was distinct but tremulous and was not slurred. There was considerable tremor of the lips and tongue. On the body were scars of tertiary syphilis. The pupils were equal and reacted normally. Knee-jerks normal.

Progress.—He became more demented, and at some time towards the end of the summer of 1896 (date not noted in the case-books of the asylum) he developed herpes zoster over the area in fig. 21, taken from a photograph. This attack left a permanent sore on his back, owing to his filthy habits and to constant scratching. He died on March 14 from pneumonia, mainly affecting the base of the right lung.

POST-MORTEM EXAMINATION.

Twenty hours after death.

On the back, in the position representing part of the area affected by the herpetic eruption, is a purplish patch of superficial ulceration. This patch lay over the posterior portion of the eleventh rib and the last intercostal space, and extended as far forwards as the anterior axillary fold.

He was well nourished and *post-mortem* rigidity was well marked.

The right pleura was thickened and adherent from recent pleurisy over the lower lobes. The whole of the lower lobe of the right lung was solid, and presented the appearance of gray hepatisation. The upper lobe was œdematous and congested.

The left pleura was normal. The left lung was somewhat œdematous and congested, but otherwise normal.

Heart normal.

Aorta somewhat atheromatous.

Liver pale, fatty, and somewhat soft.

Kidneys normal.

Spleen soft and flabby.

The brain weighed 50 ozs. (1,415 grammes). Both gray and white matter appeared normal; the ventricles were not granular, and the pia-arachnoid was not thickened or adherent and stripped well.

MICROSCOPICAL EXAMINATION.

The following parts were examined—(*a*) a series of posterior root ganglia, (*b*) a series of spinal nerve roots, (*c*) certain peripheral nerves, (*d*) the spinal cord.

(*a*) *Posterior Root Ganglia.*

The 8th, 9th and 10th dorsal ganglia were hardened in Müller's fluid and stained by Marchi's osmic acid method, by

Weigert and Weigert-Pal with hæmatoxylin, and Pal counterstained with eosin.

In no case could any change be discovered in the vessels or capsule. The method of hardening precluded the use of Nissl's method of cell staining, but the remaining methods showed no loss of cells in any ganglion.

(*b*) *Posterior Nerve-roots.*

The posterior nerve-roots of the 8th, 9th and 10th dorsal on both sides were examined by Marchi and the Marchi-Pal methods, and no change could be detected, either recent or remote.

(*c*) *Peripheral Nerves.*

The peripheral nerves emerging from the 8th, 9th and 10th dorsal ganglia on both the right and left sides were stained by Schäfer's modification (Marchi-Pal), by Marchi, and by Pal's method.

In no case was any profound change seen, except that perhaps the nerve from the 8th dorsal ganglion on the right side contained fewer fibres than that from the left ganglion on the same level.

(*d*) *Spinal Cord.*

From the level of the 11th to that of the 6th dorsal every segment was cut and stained by the (1) Marchi, (2) Weigert, and (3) Weigert-Pal methods.

In no case was there any sclerosis or acute degeneration in the posterior columns or root zones. The cord was otherwise normal.

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DESCRIPTION OF PLATES.

Plate 1.

Fig. 1.—From a coloured drawing of a longitudinal section of the 7th dorsal ganglion of the right side in a case that died eight days after the outburst of the eruption (Case 2). This section is stained with hæmatoxylin and eosin.

Fig. 2a.—From a coloured drawing of the 7th dorsal ganglion of the normal (left) side in Case 9. Death occurred 153 days after the outburst of the eruption. Stained by Marchi's method, and counterstained by van Gieson's picro-hæmatoxylin method.

Fig. 2b.—The 7th dorsal ganglion of the abnormal (right) side in the same case, stained by the same methods.

Plate 2.

Fig. 1.—Drawing from a portion of the 4th dorsal ganglion of the right side in Case 14. This ganglion was invaded by lympho-sarcomatous growth.

Fig. 2.—Photomicrograph of a portion of the same ganglion under a higher power.

Plate 3.

Fig. 1.—A low-power photograph of the 11th dorsal ganglion of the left side in Case 5. The more darkly-stained areas are foci of small round cells.

Fig. 2.—A photograph under a higher power of the inflammatory focus surrounded by a white ring in fig. 1.

Plate 4.

Fig. 1.—Photograph of one of the inflammatory foci in the 3rd cervical ganglion of the left side in Case 16.

Fig. 2.—Photograph under the same power of a portion of the 3rd cervical ganglion of the right side in the same case. Both ganglia were cut in the same block, fixed on the same slide, and stained together by Nissl's method.

Plate 5.

Case 6.

Three drawings of transverse sections of the 3rd cervical ganglia of both sides in a case in which the herpetic eruption was distributed over the 3rd cervical area of the left side.

The three right-hand figures are from the normal ganglion, those on the left from the diseased one; in the latter the pale area at the lower end of each section indicates the lesion. This area was composed almost entirely of fibro-cellular tissue, and contained no nerve-cells and no nerve-fibres.

The sections were all stained with osmic acid and hæmatoxylin for the display of nerve-fibres, and healthy fibres are indicated by black dots, the small circles representing nerve-cells.

Fig. 1 is taken from that end nearest the posterior root.

Fig. 2 from the centre of the ganglion.

Fig. 3 near to the peripheral nerve.

Abbé drawing apparatus $\frac{25}{1}$.

Plate 6.

Figs. 1a and 1b are from Case 10, and are drawn from transverse sections of the right and left 4th cervical ganglia, stained with logwood only.

In fig. 1B an extensive pallid area, almost entirely bereft of nerve-cells and nerve-fibres, is seen at the top of the drawing. This is the lesion. Fig. 1A shows the normal left ganglion for comparison. Both sections come from about the middle of the ganglion.

Abbé drawing apparatus $\frac{25}{1}$.

Fig. 2 is from Case 13, and is a drawing of the 6th dorsal ganglion of the right side. This section came from about the middle of the ganglion, and the lesion is seen lying to the right of the field. It is recognisable as a pallid area in which no nerve-cells or nerve-fibres are present, and over which the ganglionic sheath is thickened. The section was stained with osmic acid and iron alum for the display of healthy nerve-fibres, and such fibres are shown in the drawing as black dots or lines. The herpes occurred 790 days before death. The arrow points in the direction of the anterior root.

Abbé drawing apparatus $\frac{60}{1}$.

PLATE 7.

Case 7.

Four drawings, made with an Edinger apparatus, of Marchi-stained longitudinal sections of the 2nd dorsal posterior root ganglion of the left side, with annexed roots and peripheral nerve.

The first drawing illustrates a section made rather to one side of the ganglion, and shows complete destruction of the ganglionic substance (indicated by cross-hatching). The anterior root, which is normal, lies in the upper part of the field; on the right the roots pierce the dura spinalis, and the peripheral nerve is to the left, and shows signs of sclerosis (under a high power it also shows remains of degeneration).

In fig. 2, which illustrates a section more towards the centre of the ganglion, a field occupied by healthy nerve-fibres and nerve-cells is appearing in the distal segment of the ganglion.

In fig. 3 the destructive lesion is disappearing, three small foci of disease alone remaining.

In fig. 4, which is drawn from a section towards the edge of the ganglion opposite to that shown in fig. 1, the body of the ganglion appears to be normal.

PLATE 8.

The two upper figures are from Case 8, and are Edinger drawings of longitudinal sections of the 12th dorsal ganglion of the right side, stained by the method of Marchi. A typical focal lesion is seen in the upper part of the ganglionic field. Death occurred 103 days after the eruption first appeared.

The two lower figures are from Case 4, and show the appearances seen in longitudinal sections of the 12th dorsal ganglion of the left side, stained by the method of van Gieson (hæmatoxylin and picro-fuchsin). The blurred area in the upper portion of the field represents the position and extent of the ganglionic lesion. Note the hæmorrhage in the centre of the peripheral nerve in the third figure. The herpetic eruption occurred only thirteen days before death.

PLATE 9.

Case 18.

Photographs of right and left Gasserian ganglia. These photographs are explained by the underlying skeleton plan.

PLATE 10.

FIG. 1.—Twelve drawings showing the degeneration found in Case 7; it entered at dorsal 2 and was traced up to cervical 1. In dorsal 3 and 4 a few degenerated descending collaterals are indicated.

FIG. 2.—Six drawings illustrating the degeneration which occurred in Case 6; it entered at cervical 3 and was traced well up into the medulla, terminating in the nucleus cuneatus.

PLATE 11.

FIG. 1.—A series of six drawings to show the degeneration in Case 5. The degenerated fibres enter at the level of the 11th dorsal root and can be traced up to the level of the 6th dorsal.

FIG. 2.—A series of six drawings to show the degeneration in Case 3. The degenerated fibres enter at the level of the 6th dorsal root and can be traced to the level of the 3rd dorsal. A few descending collaterals are seen at the level of entry of the 7th dorsal root.

FIG. 3.—A series of six drawings to show the degeneration in Case 9. The degenerated fibres enter at the level of the 7th dorsal root and can be traced as high as the level of the 2nd dorsal. Descending collaterals can be seen at the level of the 8th dorsal root.

These drawings were made with the Edinger apparatus.

PLATE 12.

Outline drawings, made with an Edinger drawing apparatus, showing the degeneration displayed by the method of Marchi in the spinal cords of Cases 4, 8, and 17.

FIG. 1.—Six drawings from Case 4, in which the herpetic eruption was distributed over the 12th dorsal area of the left side, and the distribution of the degeneration which occurred in the corresponding posterior spinal root fibres, is represented.

FIG. 2.—Six drawings from Case 8, where the eruption also lay over the 12th dorsal area, but affected the opposite side. The degeneration in the pyramidal tracts represented in these drawings was the result of cerebral softening of thrombotic origin.

FIG. 3.—Six drawings from Case 17, in which the eruption was distributed over the 8th dorsal area of the left side and degenerated fibres enter in the corresponding posterior spinal nerve-root. This patient was a tabetic general paralytic, and the shaded area in the posterior columns indicate the site where tabetic sclerosis existed, while in the pyramidal tracts the acute degeneration commonly found in cases of general paralysis is represented.

PLATE 13.

Case 18.

Drawings to show the distribution of the degeneration in the sensory root of the right 5th cranial nerve, as brought out by the method of Marchi in a case in which the herpetic eruption was distributed over the area supplied by the inframaxillary division of that nerve.

FIG. 1 shows the entire root at its point of entry into the pons, and collections of blackened degenerated fibres are clearly visible in the outermost bundles of the sensory root. The motor root is cut obliquely and is shown lying just internal to the sensory root.

FIG. 2.—A degenerated portion of the sensory root just after entering the pons.

FIG. 3.—The sensory root in the first part of its downward course—diseased fibres cut rather obliquely. The fibres on the right are transverse pontine ones. The arrow points in the direction of the 4th ventricle.

FIG. 4.—At the level of the issuing 7th root, which is represented to the left (internal) of the 5th root. Note that there is comparatively little degeneration in the lower portion of the field.

FIG. 5.—At the level of the 8th nucleus. Between the root and the surface lie the external arcuate fibres, and on the left side internal arcuate

fibres enter and split up the root. Degeneration is still visible, and, as in the last figure, it principally occupies the upper two-thirds of the field.

FIG. 6.—At the level of the 1st cervical root the degenerated 5th root lies just below the surface external and dorsal to the substantia gelatinosa Rolandi, into the dorsal portion of which degenerated fibres stream.

Abbé drawing apparatus $\frac{25}{1}$.

PLATE 14.

FIG 1.—A photograph of a transverse section of the spinal cord of Case 9 at the level of entry of the degenerated fibres. Low power.

FIG. 2.—A photograph under a higher power of a transverse section of the spinal cord in Case 3, at the level of entry of the degenerated fibres. The lower part of this figure is towards the posterior surface of the cord; the lighter portion towards the left of the figure represents the posterior horn of the affected side.

PLATE 15.

Two Photographs of Longitudinal Sections of the Spinal Cord from Case 6.

FIG. 1.—A low-power view showing the disposition of degenerated posterior root fibres immediately after entering the cord. The periphery is on the left. The section is longitudinal and parallel with the posterior horn. $\frac{90}{1}$.

FIG. 2.—A longitudinal section of the same fibres after entering the cord. The figure gives a good idea of the degree and extent of the degeneration to be found in the cord in typical cases of zoster. $\frac{120}{1}$.

PLATE 16.

FIG. 1. Case 4.—A photomicrograph of some teased fibres of the 12th dorsal posterior root of the left side, stained by the method of Marchi. The two upper fibres clearly show acute degenerative changes. × $\frac{300}{1}$.

FIG. 2. Case 6.—A transverse section of the 3rd cervical anterior and posterior roots central to the ganglion, at the point where they pierce the dura. In the left-hand portion of the sensory root, which lies above and to the left, some sclerosed unstained bundles are to be recognised; these indicate the remains of herpetic degeneration. Healthy bundles are stained black. Method of Schäfer × $\frac{40}{1}$.

FIG. 3. Case 13.—Drawing of a transverse section of the affected peripheral nerve 1 cm. distal to the ganglion, made with an Abbé drawing apparatus from a formol-hardened osmic acid stained preparation. To the right a bundle is seen which to a large extent is deprived of nerve-fibres, and three other bundles are not quite healthy.

FIGS. 4 AND 5. Case 13.—Drawings of the above nerve more highly magnified. Fig. 4 is a portion of the healthy bundle lying to the left. Fig. 5 is a portion of the sclerosed bundle lying to the right.

A NOTE ON THE STAINING OF BRAIN IN A MIXTURE OF METHYLENE BLUE AND PEROXIDE OF HYDROGEN—A *VITAL* REACTION IN *POST-MORTEM* TISSUE.

BY JOHN TURNER, M.B.ABER.

THE oxygen of the air has such a marked effect on brains stained by Ehrlich's *intra-vitam* method, that it occurred to me to try a mixture of methylene blue and peroxide of hydrogen on *post-mortem* tissues.

The result obtained was encouraging, for to a certain extent the tissues so treated took on a "vital" staining reaction and one no longer got the usual effect of methylene-blue, there being no appearance of Nissl-bodies in the cells, and the finest ramifications of certain nerve-cell processes were displayed with great distinctness.

METHOD.

The following is an account of the method I now use, and by which good results are generally got.

Small pieces of the cortex and subjacent white matter, not more than one-eighth of an inch thick, are placed direct into a mixture of six parts 1 per cent. solution of methylene blue (patent B.X.) and one part peroxide of hydrogen solution.

The blue solution must be old; at any rate, I have not succeeded yet in getting results with a freshly-made solution. It is not polychrome, although kept exposed to light and air in a wide-mouthed unstoppered bottle for a year.[1]

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[1] This is the time that the solution I have been using was kept; but some made up only two to three weeks ago, and well aerated and exposed to sunlight, begins to give the reaction. I have also got good results from a solution made only a few months, and which had been used for staining *in toto* pieces of alcohol-hardened brain.

Very good results are obtained in the case of bodies twenty-four hours dead, and I do not think that material got quite shortly after death stains any better than that which has been dead many hours.

When the piece of brain is placed in the staining mixture a brisk evolution of gas takes place, which sometimes blows the stopper of the bottle out unless it is tied in.

After eleven days the pieces are taken out of the methylene blue mixture and put into 10 per cent. solution of molybdate of ammonia and left all day and night, then washed during the following day under a running tap till the evening, when they are placed in absolute alcohol and kept cool by running water. After a few hours the alcohol must be replaced by fresh. The pieces are left in spirit all night, and the next morning put into xylol for one hour, and then into fresh xylol for another hour, and then into paraffin for two hours, and thick sections cut. These are placed on xylol on the slide and ~~all the~~ paraffin washed out, and then decolourised for a few seconds in a mixture of equal parts of creosote and aniline oil, washed again on the slide in xylol, and mounted in Canada balsam, and the cover-glass very carefully pressed down to flatten out the section.

The staining appears to be permanent, for sections prepared two years ago show no deterioration.

In all cases the reaction is patchy, parts only of the section showing it, and these parts appear paler and generally have a faint pink tinge. I have never yet succeeded in getting the first layer of the cortex to take on the reaction.

APPEARANCES.

Cerebral cortex.—In the successful parts the ground substance is hardly coloured, the pyramidal cells (and probably the giant-cells when healthy) show no signs of any chromophilic substance, the cytoplasm of the cell (as by *intra-vitam* staining) is a pale, uniform blue, and the apex and dendrites in the vicinity of the cell-body are similarly coloured, but in some cases at a little distance they both stain densely. The nucleus in these cells appears very prominent and plump ; it is strongly outlined and filled with dark granules, so that it is by far the darkest part of the cell. The nucleolus is often obscured; when visible it is *pale* and ill-defined in healthy cells (see figs. 4 and 5).

Around these cells, and extending along the apex and dendrites, are seen a number of fine beaded fibrils, arranged as a network all over the cell-body and its processes (see figs. 1 to 5). The branches of this network appear to be given off from the beads, and not from intermediate portions of the fibres (fig. *C*).

This appearance was fully described by Drs. W. A. Turner and W. Hunter, as seen after *intra-vitam* staining of animals' brains.[1]

It has never hitherto, as far as I know, been demonstrated in the human brain.

The beaded fibrils can be seen arriving at the nerve-cells from different places; some pass on to the apex here and there along its course, coming from the adjacent matrix, others similarly to the dendrites, and the fibrils from these different sources appear to anastomose into a continuous network which, as before said, envelopes both the cell-body and its extensions.

I have been able to follow this arrangement for a considerable distance over the apex and along outstanding dendrites (fig. *B*).

Besides the above-described pale cells, others (see fig. 5) are seen, relatively few in number, which stain very darkly indeed, both the body of the cell and its processes to their furthest ramifications.

These cells are generally small and pear-shaped or multiangular, and they occur in all but the first layer of the cortex.

Although my tissues were from diseased subjects, yet, as these cells occur in all of them, and as they are mentioned by W. A. Turner and W. Hunter as seen in the animals they experimented on, they may with considerable certainty be taken as representing a normal type of cell.

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[1] "A Form of Nerve Termination," by Drs. W. A. Turner and W. Hunter, BRAIN, Spring Number, 1899.

Now the processes of these cells, which can often be followed for 200 or more μ, are at first shaggy in outline, and as they get smaller they present little varicose swellings along their course, and eventually in their finest divisions they appear identical to the beaded fibrils which form the network about the pale pyramidal cells. In some cases, where a dark and a pyramidal pale cell have been favourably situated in the section, I believe I could directly trace the beaded dendrite into the beaded network, but as the fibrils we are dealing with are so excessively fine, it is impossible even with a one-twelfth oil immersion to be certain on this point (fig. *A*).

Drs. W. A. Turner and W. Hunter derive this beaded network from the terminal branching of collaterals given off from the axons of other cells, and not from dendrites as above described.

In my preparations the axis cylinders, as seen in the white matter adjacent to the cortex and where they course up through the lower part of the cortex, always appear smooth in contour and very pale. This to a certain extent corroborates the supposition that the darkly-stained fibrils of the network comes from the similarly darkly-stained dendrites of the small darkly-stained cells. But as we have seen that sometimes the processes of pale pyramidal cells take on a dark stain at a certain distance from their parent cell, it is quite possible that the collaterals also may stain deeply although the axis cylinder stains lightly. Apart from this, however, I think that the similarity of the fine branches of undoubted dendrites with the fibrils forming the beaded network, is a very strong point in favour of the supposition that the latter is an extension of the former.

Given off from the sides of the shaggy dendrites of the dark cells are very fine lateral processes which may end in a bead, or may have more than one in its course; possibly these represent the thorns and gemmules of silver preparations (figs. 6 and *D*).

Cerebellar cortex.—So far I have done very little with this part, but the sections from a fairly successful specimen showed a number of smoothly contoured wavy fibres running parallel to the plane of the section (which was from a piece of tissue cut in a sagittal direction from the cerebellum) in the lower fourth of the molecular layer.

Among these fibres could be seen an occasional small (12 μ) darkly-stained pear-shaped cell, from which processes which appeared identical to the above-mentioned fibres were given off from either end.

These fibres give off right-angle branches at intervals running towards the granular layer.

Similar fibres course along the branches of the Purkinje cells and pass over the cell body in a longitudinal direction, forming a basketwork around it, and this basketwork often appears to end in a dense cluster a little distance beneath the cell, exactly as described and illustrated by Dr. Alexander Hill.[1] I have not noticed any anastomosing branches between the fibres around the Purkinje cells, and they show no signs of beads. Perhaps they are not nerve but neuroglia fibres?

Although the method here described is capricious and uncertain in its action, yet it shows the possibility of staining in *post-mortem* tissue delicate structures which have hitherto only been revealed by methods inapplicable to human subjects.

We may, I think, reasonably expect that with further experience, and when we know more about the conditions on which the staining depends, to get more certain results.

Even in its present imperfect state it may enable us to further unravel the very complicated inter-communications which exist between nerve-cells, and possibly it may prove of service in studying the pathology of the nervous system.

ADDENDA.

No. 1.—It is advisable to take out the stopper of the bottle containing the staining mixture and the piece of brain occasionally to let out the gas evolved, and to shake up the solution from time to time.

No. 2.—Further trials make it probable that the reaction depends to a large extent on the length of time the tissue is left in the staining fluid.

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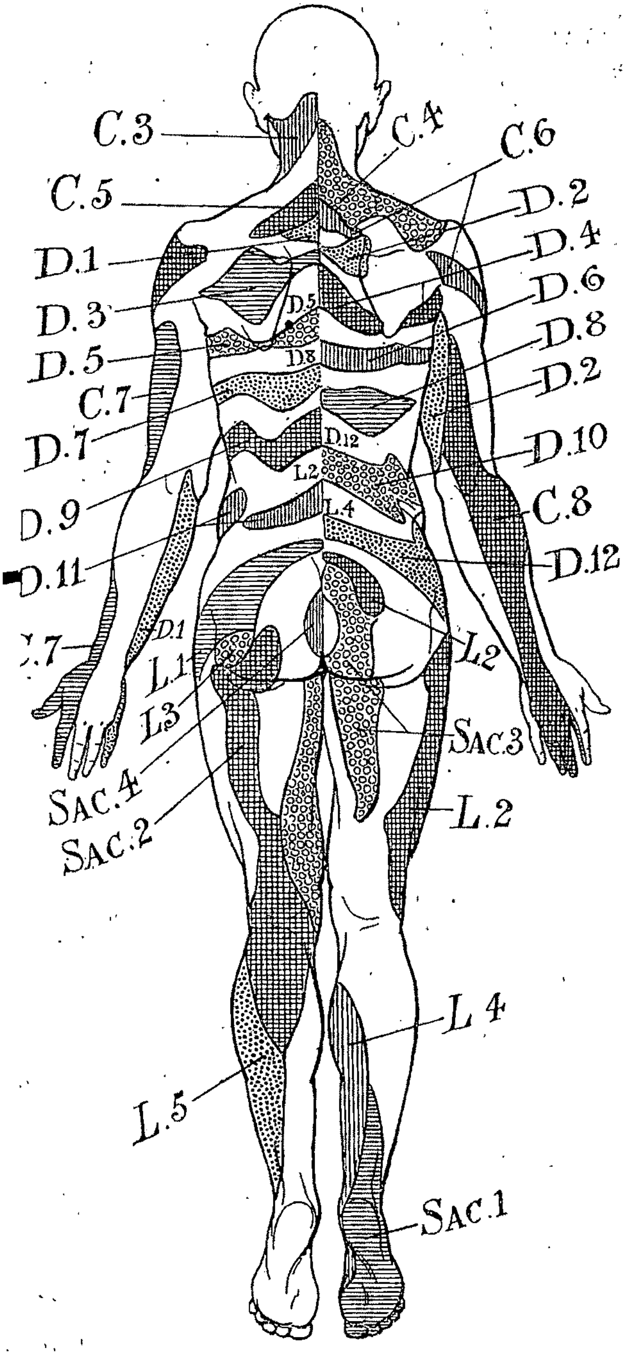
[1] BRAIN, 1896, xix., pp. 22-25, fig. 6.


C.3
C.4
C.6
C.5
D.2
D.1
D.4
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D.5
D.6
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D8
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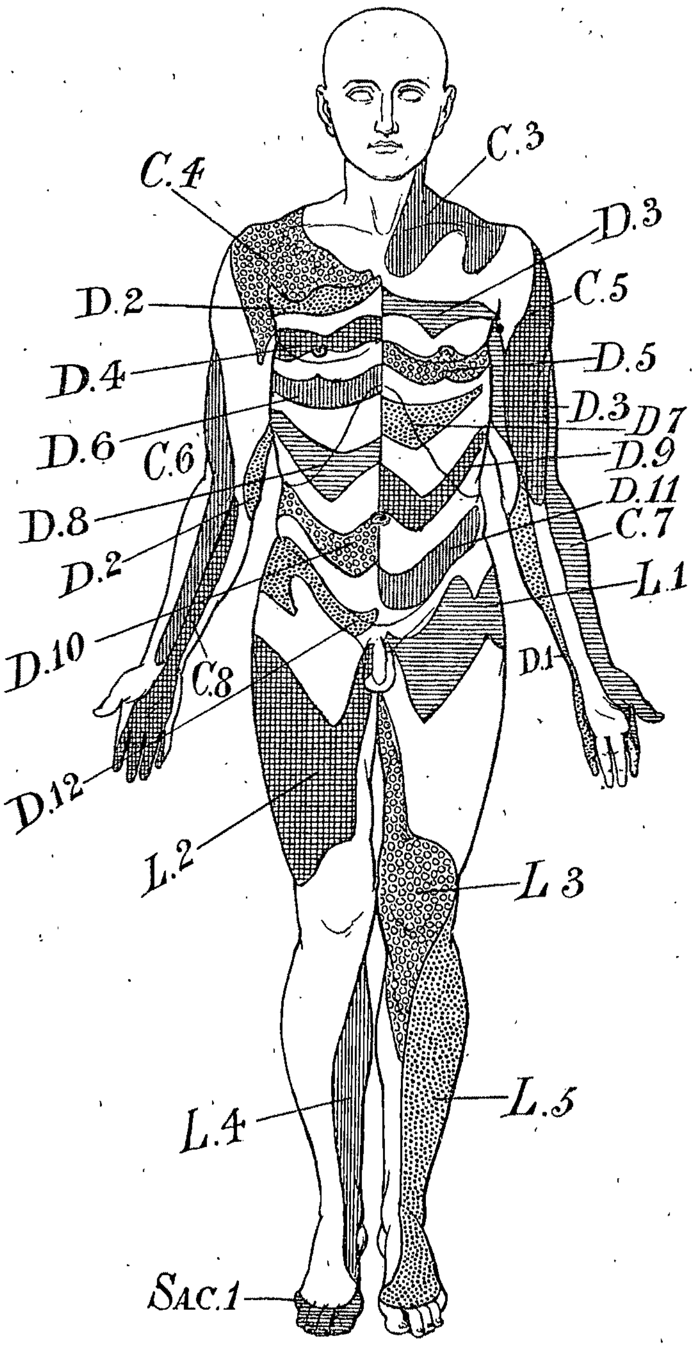
C.7
D.2
D.7
D.12
D.10
L2
D.9
L.4
C.8
D.11
D.12
D1
L2
C.7
L.1
L3
SAC.3
SAC.4
L.2
SAC.2
L 4
L.5
SAC.1


C.4
C.3
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C.5
D.4
D.5
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D 7
D.6
C.6
D.9
D.11
D.8
C.7
D.2
L.1
D.10
D.1
C.8
D.12
L.2
L 3
L.4
L.5
Sac.1

PLATE 17.

An attempt to represent on one diagram the areas occupied by the eruption of herpes zoster. Of the areas here represented the following have been confirmed by microscopical examination :—

Cervical 3.—(Case 6 and Case 17.)
Cervical 4.—(Case 10.)
Dorsal 2.—(Case 7.)
Dorsal 4.—(Case 11 and Case 14.)
Dorsal 6.—(Case 3 and Case 13.)
Dorsal 7.—(Case 2 and Case 9.)
Dorsal 8.—(Case 16.)
Dorsal 11.—(Case 5.)
Dorsal 12.—(Case 4, Case 8 and Case 12.)
Lumbar 1.—(Case 1.)

Thus we consider that the areas on the neck and trunk are more likely to be correctly mapped out than those on the limbs. Moreover, the difficulty in determining the distribution of these areas on the limbs is heightened by the rarity of zoster on the extremities (*vide* p. 394).

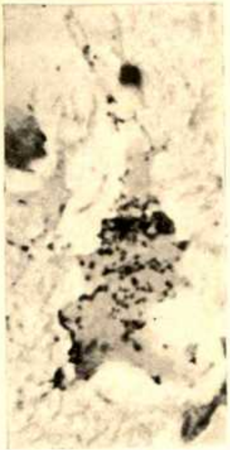


FIG. 1.

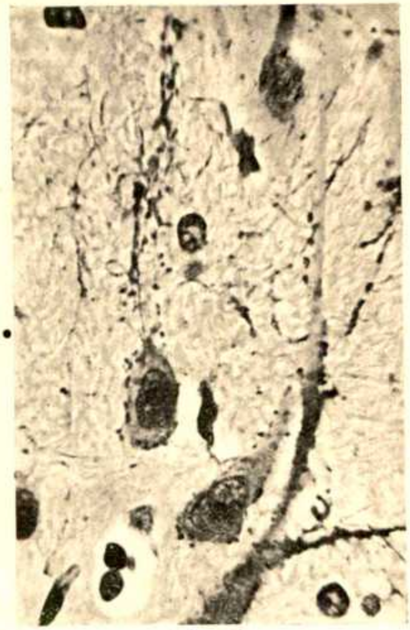


FIG. 2.

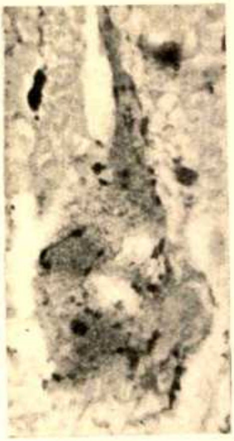


FIG. 3.

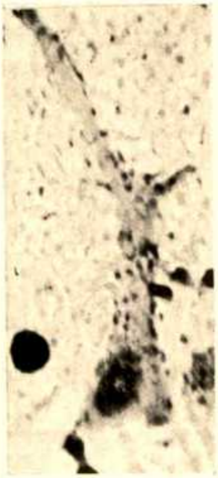


FIG. 4.

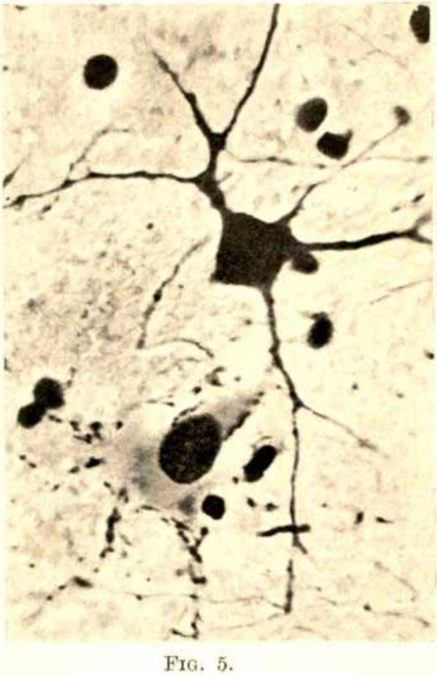


FIG. 5.

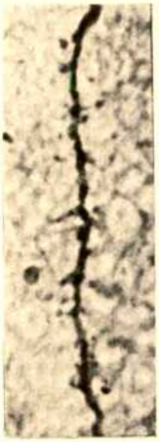
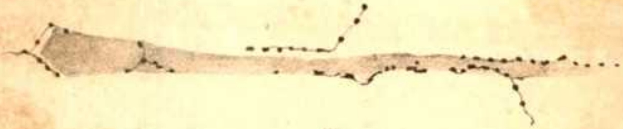


FIG. 6.

A



B

C

D

Bale & Danielsson, Ltd., Lith.

I have got a reaction in pieces of brain left eleven days, whereas in other pieces of the same brain left only four days no result was obtained.

Methylene blue solutions are preservatives of brain, so that no decomposition takes place even after weeks in the solution.

No. 3.—Since the above account was written I have observed beaded fibrils quite similar to those seen around the cerebral cells forming a network around the Purkinje cells of the cerebellum.

DESCRIPTION OF FIGURES.

No. 1.—A giant-nerve cell, the body of which is out of focus, showing the beaded network surrounding it. × 600.

No. 2.—Three pyramidal cells; in the uppermost the beaded network is seen over the apex and all round the cell body. The beads are also clearly visible along the sides of the other two cells. × 600.

No. 3.—A giant-nerve cell, out of focus, showing portions of beaded network upon it. × 600.

No. 4.—A pyramidal cell with pale uniform cytoplasm, dark nucleus, and pale irregularly-outlined nucleolus. Beads are seen on the cell-body and apex, but the connecting fibrils are not visible in the photograph, although seen in the section from which it is taken. × 600.

No. 5.—Small darkly-stained cell with processes of irregular contour, also a pale pyramidal cell with dark nucleus. The beaded network is shown at the edges of this cell and over its dendrites. × 600.

No. 6.—A delicate darkly-stained nerve-fibril with lateral projections and beads. × 1,200.

Note.—No two of the figures of nerve-cells are from the same case.

A shows a darkly stained cell with a shaggy dendrite passing to, and apparently breaking up into beaded fibrils around a pale cell.

B.—Apex of a pale cell with beaded fibrils about it.

C.—Beaded network over a pale cell (the cell is not figured). The nutrient vessel of the cell is seen.

D.—Two fine fibrils with fine lateral beaded processes.

REPORT ON A SUBDURAL BLOOD CYST.

BY J. O. WAKELIN BARRATT, M.D., B.SC.LOND., F.R.C.S.ENG.

Pathologist to the West Riding Asylum, Wakefield.

THE condition about to be described is of great pathological interest, being occasionally and, on the whole, rarely met with in asylums, and still more rarely in workhouse infirmaries and hospitals.

CLINICAL HISTORY.

Patient was a male, 57 years of age, whose mental condition (dementia) was stated to have been developing during the previous two years. On admission, he was found to be extremely demented and very restless, and could only with difficulty be induced to reply to questions. If pressed to answer he would commence to groan and become emotional. He showed great lack of intelligence, but was able to feed himself. He was feeble, emaciated, and anæmic. Tongue not tremulous. Pupils equal. Knee-jerks present. Some incontinence of urine. The area of superficial cardiac dulness was enlarged, a systolic bruit was present at the heart's apex, and the arteries were thickened. Breath sounds faint. Urine pale, acid; specific gravity, 1015; contained albumen.

The patient, after admission, continued restless and feeble-minded. At the end of a week it is noted that he appeared to have had a slight stroke, affecting the left side. There was much rigidity about the shoulders, but he was able to move his arms. Head and eyes turned to the right. Constant dribbling of urine. Mentally there was complete dementia.

Four days later it was noted that the hemiplegic symptoms had passed off, but the mental condition remained unchanged.

At the end of another week it was observed that there was a good deal of rigidity about the left arm, especially at the shoulder. Nothing could be got out of him; he lay in bed, groaning at times, but taking nourishment fairly. He continued in this condition until his death occurred, twenty-two days after the left-sided weakness had been noted. Shortly before death some râles were observed at the bases of the lungs posteriorly.

Patient's occupation was that of a driller.

There were no epileptiform attacks, nor any anasarca or ascites during patient's stay in the asylum.

The above is an abstract of the case-book notes (for which I am indebted to Dr. C. W. Ensor). The following additional information was subsequently obtained from the patient's wife.

Patient's father died at 62 years of age, of dropsy; he had "fits" lasting two or three weeks at 50 years of age, but not subsequently. Patient's mother died at 42 years of age, of some lung trouble. Patient had no brothers, but two sisters, both dead, one of typhoid and another of an illness attributed to a bad smell from a drain. No other near relatives. No consumption or gout in family.

Patient was a quiet man, employed all his life as a mechanic at a locomotive engine works. He was a steady worker. He drank little, on the average not more than two glasses of beer a week. Did not take spirits. Was averse to drink, which made him excited, because it caused him to suffer subsequently from bad headaches. Did not smoke much. Never had any fever nor sunstroke (except the illness occurring thirteen years ago, described below, is of this nature). No injury to the head, no exposure to lead, no winter cough, never suffered from squint or weakness of a limb. Never had any fits. Was ruptured at 16 years of age, and always wore a truss.

Patient was married at 26 years of age. His wife had three miscarriages after marriage; the first at about four months' pregnancy, the second and third at about six months'; she did not subsequently become pregnant. The wife's health has always been good. Three weeks after marriage patient was troubled with a sore throat; he had much pain, and remained in bed four or five days, but there was no hoarseness or loss of voice.

Patient was subject to headaches all his life.

Twenty-four years ago patient had an illness lasting several weeks, the nature of which is not clear; complete recovery occurred. Thirteen years ago had another attack of illness of doubtful nature, not apparently severe, from which he recovered at the end of two or three months. During this illness the left shoulder was the seat of much pain.

Another attack of influenza occurred six years ago. Patient was ill seven weeks. Complete recovery occurred.

Three years and ten months ago patient had a second attack of influenza. He remained in bed for eight weeks. He had much pain in the back, particularly in the lumbar and sacral regions. When he left his bed he was unable to move about much. He tried to work, but was unable to do so, because of the pain in his back. He used to get excited and lose his temper, and would follow his wife about like a child. About this time he used to have cramp in the calf-muscles; and he suffered from sore throat, which left him hard of hearing. A change occurred in his disposition. He became emotional, would strike his wife without any cause, and exhibited suddenly, according to his wife's account, difficulty of speech, that is to say, he tried to speak, but could not. Patient, when this occurred, became quite prostrate; next day he was restless, getting in and out of bed, and he exhibited much mental defect, being unaware of the time of day and not knowing what was going on around him. He passed his urine and fæces into the bed.

Patient was removed into the workhouse infirmary three months after the commencement of the second attack of influenza. Here, according to the statement of his wife, who visited him regularly, his condition got on the whole steadily worse, though at times some improvement occurred, followed by a change for the worse. At first he appeared to gain flesh, but this may have been merely apparent, for his face became puffed up, and the abdomen swollen, both of which his wife attributed to "dropsy." Most of this time he was in bed, but sometimes he walked a little about the ward, the last occasion being about two months before admission to the asylum. When he moved about the ward his wife did not notice any weakness of the limbs on one side of the body, nor did she at any time notice any disorder of gait. During his stay in the workhouse infirmary patient was never able to recognise his wife.

POST-MORTEM EXAMINATION.

Some difficulty was experienced in removing the skull-cap, which was thin but dense, owing to the existence of adhesions on the part of the dura mater. This membrane, which was not thickened, exhibited on its inner surface a thin yellowish-brown pellicle at the base and on the left side over the vertex, while on the right side a large moderately firm flattened sac of a dark reddish-brown colour lay in the subdural space over the cerebral hemisphere, which was considerably flattened (figs. 1 and 2). This sac was about 14 centimetres long by about 10 centimetres broad, and had a maximum thickness of 2½ centimetres. At the edges it thinned off and became continuous with the rusty pellicle already referred to. Its contents consisted partly of a friable, brownish-black, soft solid material, and were in part made up of a dark-brown fluid not draining away readily when the sac was incised. The wall of the sac was firm and of a grayish-brown colour; it was rather firmly adherent both to the dura and to the pia arachnoid, so that some difficulty was experienced in separating it from these membranes. The thin rusty pellicle, on the other hand, was closely adherent only to the inner surface of the dura mater.

The falx cerebri was considerably displaced to the left (figs. 1 and 2). This displacement, which was striking in its aspect both when viewed from above (fig. 1) and in frontal section (fig. 2), was most marked opposite the middle of the vertex, where also the sac was thickest. The pia arachnoid was slightly thickened and opaque, chiefly over the vertex. The subarachnoid space contained clear yellowish fluid, and the sulci lying between the cerebral convolutions were widened. The gyri were wasted.

On making a frontal section of the cerebrum and the subdural formation after hardening (fig. 2), additional information concerning the formation of both was obtained. The wall of the subdural sac was well defined and sharply limited from its solid and semifluid contents. Its general thickness, which was fairly uniform, was about 1 millimetre. At the angle of junction of its outer and inner surfaces, however, it was much thicker, as is seen in the second figure. The contents, after hardening, were in part solid, exhibiting an imperfectly stratified arrangement and very friable, and in part consisted of fluid containing solid particles freely suspended. On the surface of the sac turned towards the hemisphere sinuous grooves were seen which corresponded to the large veins observed on the surface of the brain. Along these grooves, which were well seen before, as well as after, hardening, the surface of the sac was whitish in aspect.

The cerebrum was displaced to the left by the subdural cyst, both hemispheres being alike affected, and the structures, which are normally mesial in position, lay to the left of the middle line (fig. 2). The alteration in form was greatest on the right side, where the hemisphere was considerably flattened on its upper and outer aspect. The island of Reil was especially distorted on this side. The basal ganglia and the third and lateral ventricles were also markedly and unequally distorted. The corpus callosum is shown in the section to be displaced to the left.

The ventricles, like the subarachnoid space already described, were somewhat dilated, the distension, however, not being considerable (fig. 2). Thus, in addition to the presence of a large sac in the subdural space and the corresponding amount of brain atrophy which this causes, there is an additional degree of atrophy revealed by the excess of fluid in the ventricles and subarachnoid space. It is not, however, possible from the pathological appearances to determine how far the loss of brain substance is to be regarded as due to the presence of the subdural sac and how far it is to be viewed as part of the change in the brain so frequently found in senile dementia.

No focal lesions were found in the encephalon. The cerebellum was adherent to the dura mater, covering the posterior fossa on the left side. The spinal cord presented no naked-eye change.

The weight of the entire brain was 1,040 grammes; the cerebellum weighed 110 grammes; the pons and medulla 15 grammes; and the subdural sac 115 grammes.

The arteries at the base of the brain were healthy, as were also the venous sinuses.

The lungs were congested and œdematous at both bases. The mitral and tricuspid valves of the heart were thickened. The heart-muscle was firm. There was commencing atheroma at the root of the aorta. The kidneys showed some degree of chronic interstitial nephritis. The remaining viscera showed no gross change.

Inguinal hernia was present on the right side. There was marked phimosis. There was no distinct scar on the penis, nor any punched-out scars on the body, nor any thickening of the ribs or of the long bones of the limbs.

The body was much emaciated.

MICROSCOPICAL EXAMINATION.

A section of the wall of the sac shows it to consist of fairly dense connective tissue, containing an abundance of blood-vessels, a large number of which are of considerable size and very thin walled, together with numerous cells (figs. 3, 4, and 5).

The connective tissue strands are for the most part arranged parallel to the surface and intersect each other at all angles. They vary much in size, from the finest threads to relatively coarse bundles (fig. 5). Lying upon them are large flattened elongated nuclei, round which no well-defined cell protoplasm can be recognised.

The blood-vessels of the sac wall are numerous and of very varying size. A striking feature is the number of dilated vessels with very thin walls which are seen, particularly in the middle layer of the sac-wall (fig. 3). Occasionally, but far less frequently, a small vessel can be recognised the lumen of which is narrowed. The contents of the vessels consist usually of red blood-cells, not differing in aspect from those seen in the cavity of the sac in immediate contact with its inner surface. Mixed with the red cells in the blood-vessels are a small number of mononucleated and multinucleated leucocytes. In addition, however, and particularly in the neighbourhood of the more abundant cell infiltration, cells, usually mononucleated, of large size, with abundant cell protoplasm, closely resembling those outside the vessels, are encountered in the blood contained in the blood-vessels of the sac-wall.

The cells lying in the meshes of the connective tissue of the sac-wall are free or loosely adherent to the connective tissue bundles or to each other. Occasionally they are arranged in rows of two to four (figs. 4 and 5), but more frequently are seen in the section to be more or less isolated. Some of the cells are of small size, and possess little cytoplasm; this is especially the case near the inner surface (fig. 3). Others are of considerable size, reaching 40 μ or 50 μ in diameter. The increase in size generally affects the nucleus, but is chiefly caused by the abundance of cell-protoplasm (figs. 4 and 5). The cytoplasm is somewhat granular in aspect, and in some, but not all, of the cells contains masses of brownish-yellow pigmented material, which is tinted by protoplasmic stains and but little affected by nuclear dyes. This pigment is always arranged in little masses, and never appears diffused through the cell-protoplasm. It is clearly derived from red blood-cells, the remains of former hæmorrhages, and the cells in which it is found are macrophages. The amount of pigment which the cells contain varies considerably. It is absent from the smallest cells, and is generally most abundant in the largest cells, in which the nucleus stains badly, or may be unrecognisable (fig. 5). Nevertheless, some of the largest cells which the sac-wall exhibits may be quite free from pigment masses (fig. 4). Pigmented cells are found of large size and in large numbers in the middle of the sac-wall, but they are also present elsewhere, and can be recognised in the blood clot lying in immediate contact with the inner surface of the sac. The nuclei of the cells lying in the meshes of the connective tissue of the sac-wall are usually single and more or less rounded or oval in shape. Sometimes the nuclei are irregular in shape, and occasionally mononucleated cells, generally of small size, are seen.

Immediately in contact with the inner surface of the sac blood clot is found. This is little altered in aspect from that seen in the dilated vessels of the sac-wall. The red blood-cells preserve their form well. Penetrating for a distance of one-eighth to nearly one-half a millimetre, delicate blood capillaries are seen in the blood clot (fig. 3). These are accompanied by free cells. Beyond this distance few nuclei can be seen, but some ill-defined band-like structures are visible, the nature of which is not clear (fig. 3). No hæmatoidin crystals can be found near the inner surface of the sac-wall. In the central parts of the sac-cavity the solid or semi-solid material present cannot be satisfactorily sectioned in thin layers. Sometimes connective tissue strands are recognisable, extending into the clot, but they are not abundant.

No bacteria could be recognised in the sac-wall or blood clot lying on its inner surface, on staining by Loeffler's, Gram's, or Ziehl-Neelson's methods. The pia arachnoid membrane, similarly examined, exhibited no bacteria.

The pia arachnoid was found to present an excess of connective tissue, the strands of which were coarse and contained numerous blood-vessels, together with an abundance of cells, usually mononucleated and containing a fairly large amount of cell-protoplasm, the largest being 20 μ to 25 μ in diameter.

The cerebral cortex exhibited some thickening of many of the blood-vessels contained in the gray matter. There was no marked increase in the neuroglial nuclei. The nerve-cells in the gray matter of the motor area did not appear much altered in aspect by v. Gieson's stain. Minute examination by Nissl's method could not be made, owing to the method of hardening adopted.

The optic nerves, stained by Marchi's method, gave evidence of degeneration, not intense in degree (fig. 6). There appeared to be some thickening of the connective tissue septa and nuclei of these nerves.

The spinal cord showed, by Marchi's method, some degeneration in the crossed pyramidal tracts, especially on the left side. By Pal's method also the spinal cord exhibited slight, but distinct, sclerosis of the crossed pyramidal tracts and also in the posterior columns.

REMARKS UPON THE PRECEDING OBSERVATIONS.

The following points in connection with this pathological condition are worthy of note.

As already stated, two morbid processes are present within the skull cavity; the brain exhibits an atrophied wasted condition, with opacity of the pia arachnoid and fluid distension of the subarachnoid space and ventricles, such as is so commonly found in asylum patients advanced in life, suffering from dementia; and in addition there is a subdural formation of large size, assuming the form of a cyst with well-formed wall and partly fluid contents. There is, therefore, a difficulty in the way of deciding how far the clinical symptoms which the patient presented should be attributed to the former and how far to the latter condition. The left-sided weakness and the degeneration of the crossed pyramidal tracts in the cord, chiefly on the left side, appear to be almost the only symptom and change which can with certainty be attributed to the subdural cyst. Previous to his removal to the workhouse infirmary, and also during his stay in the asylum, patient did not suffer from vomiting, nor did head pain appear to be, at any rate, an obtrusive symptom. There was, however, degeneration in the optic nerves, not marked in degree, so that optic neuritis must have been present during life.

The morbid process taking place in the subdural space is the condition of hæmorrhagic pachymeningitis, complicated by the occurrence of an unusual amount of hæmorrhage. The blood poured out has become encapsuled by the formation of fibroid tissue, both on its dural and on its pial aspect. At the edges the sac-wall becomes continuous with the rusty pellicle found elsewhere on the inner surface of the dura. That the process is of old standing is shown by the large amount of connective tissue which the wall of the sac contains. It is probable also, from the richness of the sac-wall in large-walled blood-vessels and from the abundance of cells which it contains, that the morbid process is progressive, and therefore it is likely that the effused blood which subsequently became encysted was not poured out on a single occasion, but was the result of several successive hæmorrhages.

In its microscopical characters the cyst-wall resembles the subdural membranes ordinarily met with, consisting as it does of a connective tissue framework containing numerous cells in its meshes together with very many large thin-walled blood-vessels. The cells, however, are much larger in size than those usually seen in the blood-stained membranes lying on the inner surface of the dura mater, and the existence among them of macrophages in larger numbers than is generally the case in the latter is a striking feature. On the inner surface of the sac-wall the penetration of the blood clot lying within the cyst cavity by newly-formed capillaries accompanied by free cells is also beautifully seen. Connective tissue is later in its appearance in the blood clot than is the formation of new capillaries.

The formation of a blood cyst in the subdural space is a comparatively rare complication of hæmorrhagic internal pachymeningitis, though flattened hæmorrhages, not surrounded by a defined fibroid wall, are not rarely met with when subdural membranes are present, and may have a diameter of several centimetres.

The condition of the cerebrum is, by itself and apart from the distortion caused by the pressure of the blood cyst, indistinguishable, as already indicated, from that present in the brains of senile dements. Nevertheless, the extreme effusion of blood in the subdural space must be considered to have had a share in the production of the brain atrophy. How great this share is cannot, however, be gauged.

Both morbid conditions are very advanced. It has already been mentioned that the sac weighed 115 grs., while the weight of the entire brain was 1,045 grs. Nevertheless, the whole of the skull cavity was not occupied by brain and cyst together, room being still left for fluid in the subarachnoid space and ventricles.

DESCRIPTION OF THE ILLUSTRATIONS.

Fig. 1.

The brain seen from above, the subdural sac lying upon the right hemisphere having been removed. The sketch, made after hardening, shows the displacement of both hemispheres caused by the sac. The great longitudinal fissure is pressed over to the left of the mesial plane, especially in the middle of its course, being thus concave to the right. The right hemisphere is considerably flattened. The sulci are widened on the left side, but on the right, owing to the flatness of the surface, they are less distinct and assume a somewhat linear character.

R.R.; fissure of Rolando. *S.S.*; right Sylvian fissure (posterior limb). Three-quarters of the natural size.

FIG. 2.

Frontal section of brain and subdural cyst, made between the optic chiasma and the corpora mammillaria. To the right is seen the cyst lying flattened out upon the right hemisphere. Its wall is of fairly uniform thickness of one millimetre or a little less except at the edge of the cyst, where its right and left portions meet, and where its thickness is much increased. In this situation the sac-wall becomes continuous with a thin rusty pellicle lying adherent to the inner surface of the dura mater, beyond the limits of the cyst. The cyst contents are partly solid, having in places an imperfectly stratified character, and in part consist of fluid containing particulate matter evidently derived from effused blood.

Both hemispheres are distorted in shape, the longitudinal fissure and corpus callosum being displaced to the left. The islands of Reil and the basal ganglia are altered in outline as shown in the figure. Both lateral ventricles and also the third ventricle are seen to be slightly dilated, as is also the anterior extremity of the right inferior cornu, which passes more forward than its fellow, and is therefore seen in the section. The subarachnoid space is distended with fluid, and the sulci are widened. Below the third ventricle a portion of the tuber cinereum is seen, and on each side are the optic tracts. On either side of the third ventricle is seen the corresponding optic thalamus, external to which lie the lenticular nuclei, each showing several divisions. Still more externally lie the outer capsules and the claustra, opposite which are the islands of Reil, and the posterior divisions of the fissures of Sylvius. Between the lenticular and caudate nuclei on each side is seen the internal capsule, above which is seen the tail of the caudate nucleus. Below each globus pallidus is seen the nucleus amygdalæ.

R.R.; fissure of Rolando. On the right side portions of this fissure are cut across in three places. Three-quarters of the natural size.

FIG. 3.

Section of the wall of the blood cyst, together with a portion of the contents lying in contact with its inner surface. The cyst-wall is made up of stout connective tissue bundles, well supplied with blood-vessels, which towards the upper part are of large calibre and thin walled (their contents have dropped out during the preparation of the section). Between the strands of connective tissue are cells of various kinds, especially numerous in the middle of the cyst-wall and at its inner surface. In the former situation the cells are frequently of large size, sometimes deeply staining, sometimes staining faintly, and not unfrequently loaded with brownish-yellow pigment. Towards the inner surface the cells generally are of small size. In all parts of the sac-wall elongated nuclei are recognisable, not surrounded by well-stained protoplasm, lying upon the connective tissue strands. In the blood clot, in contact with the inner surface of the cyst-wall, numerous capillaries can be recognised together with free cells. Deeper down the number of nuclei recognisable is considerably diminished. Some ill-defined band-like structures are also seen in the blood clot, the nature of which is not clear.

Stained with methylene blue. × 80.

FIG. 4.

Portion of wall of subdural cyst. The sketch shows an abundance of connective tissue strands, more or less wavy when cut longitudinally, in the meshes of which a number of cells showing much granular protoplasm are seen. Generally these cells are quite free; less frequently several cells are found in contact with each other, forming a string of two to four cells. Two of the cells contain pigment masses, but with this exception the cells are free from pigment. (In other situations the same section shows large numbers of cells with pigment, as in the next figure.)

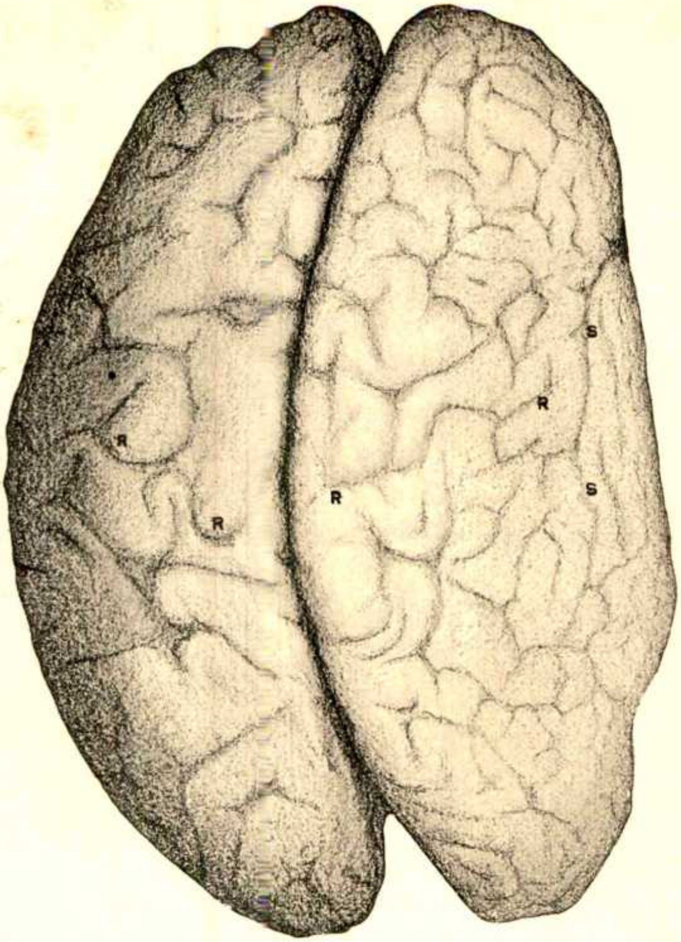


FIG. 1.

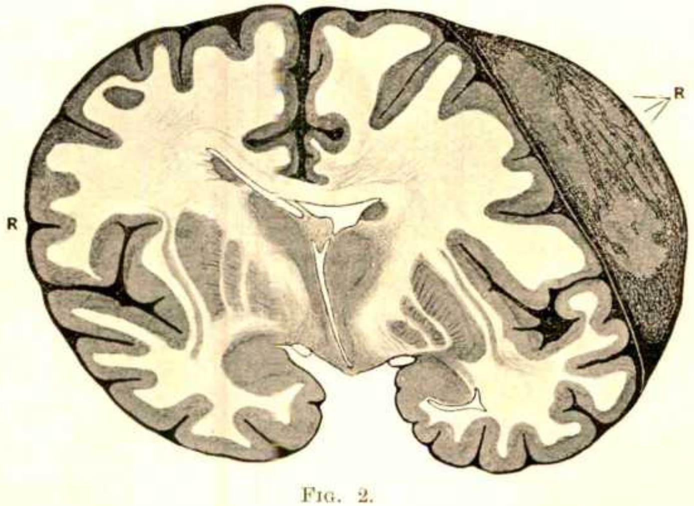


FIG. 2.

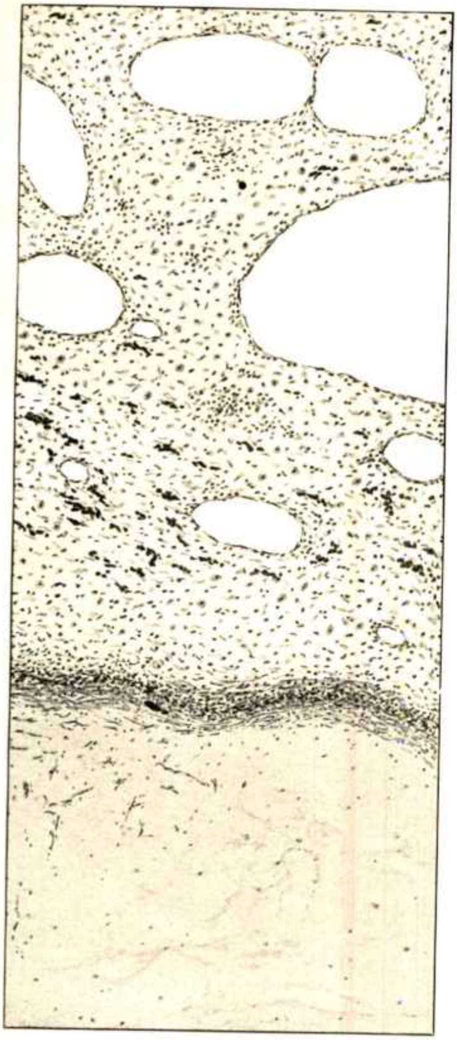


FIG. 3.

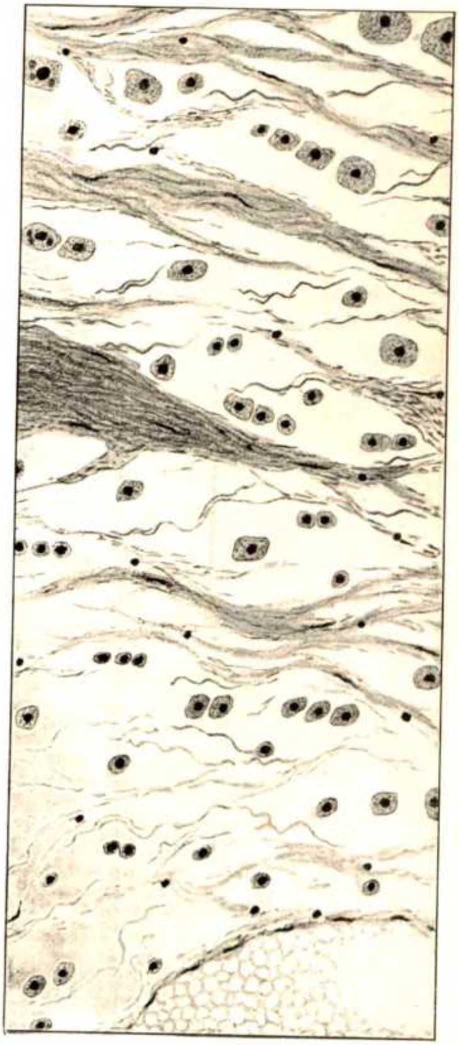


FIG. 4.

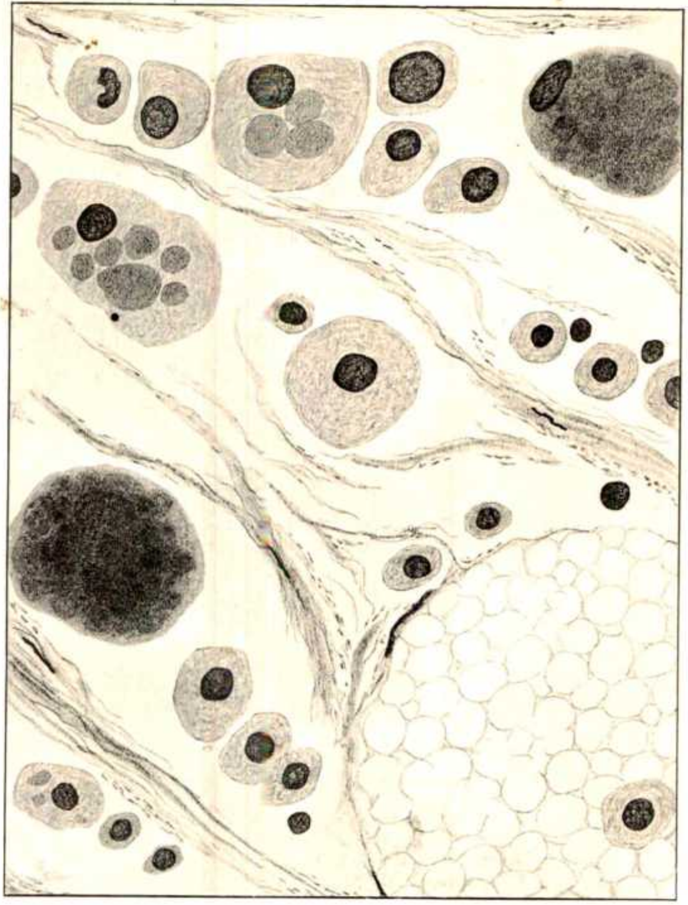


FIG. 5.

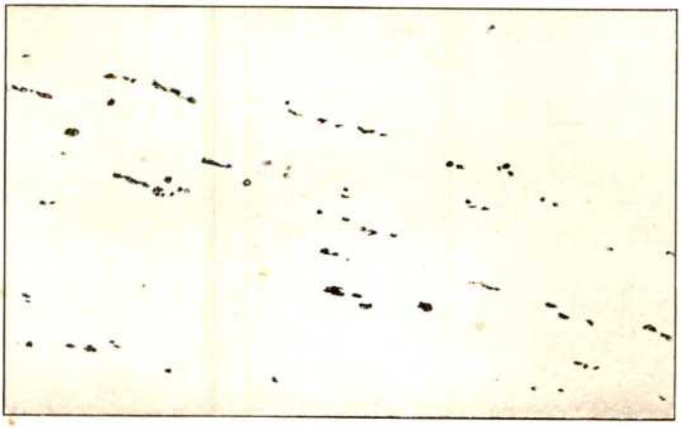


FIG. 6.

In addition, flattened elongated nuclei are seen in small numbers lying against the collagen strands.

In the lower part of the section part of a blood-vessel is seen.

v. Gieson's stain. × 200.

FIG. 5.

Wall of subdural cyst more highly magnified than in the preceding figure. The section exhibits a number of large cells (macrophages), the cytoplasm of which contains masses of pigment of varying size, of a yellowish-brown or yellowish-red colour. Where the pigment is very abundant the nucleus ceases to be recognisable. Some of the cells, especially those of small size, are free from pigment. Transitional forms are also seen. It will be noted that the nuclei of the smaller cells are smaller than those of the larger, but the difference between the two depends essentially upon the amount of cytoplasm, which is disproportionately greater in the large than in the small cells. The cell-protoplasm when free from pigmented material is of a finely granular aspect, and stains brown. No matter how abundant the pigmented material is, it remains in the form of small masses and does not become diffused through the cell-protoplasm.

Connective tissue strands are seen, cut across longitudinally, obliquely and transversely. Applied to these are seen in profile elongated flattened nuclei. In the lower right hand corner is seen a blood-vessel cut across transversely.

v. Gieson's stain. × 550.

FIG. 6.

The right optic nerve stained with osmic acid. A small amount of fatty *débris* is seen, the black particles being arranged parallel to the direction of the nerve-fibres.

× 250.

PROCEEDINGS OF THE NEUROLOGICAL SOCIETY OF LONDON.

Physiological Laboratory, St. Mary's Hospital, October 25, 1900.

Abstract of Dr. A. D. Waller's communication,

"ON THE EXCITABILITY OF NERVOUS MATTER: ITS LAST SIGN OF LIFE."

References to previous papers :—

No. 1.—"On the Excitability of Nervous Matter, with especial Reference to the Retina."—BRAIN, 1900, p. 1.

No. 2.—"On the Retinal Currents of the Frog's Eye, excited by light and excited electrically."—*Phil. Trans. R. S.*, 1900, March 29.

No. 3*a*.—"The Electrical Effects of Light upon Green Leaves." —*Proceedings R. S.*, 1900, June 6.

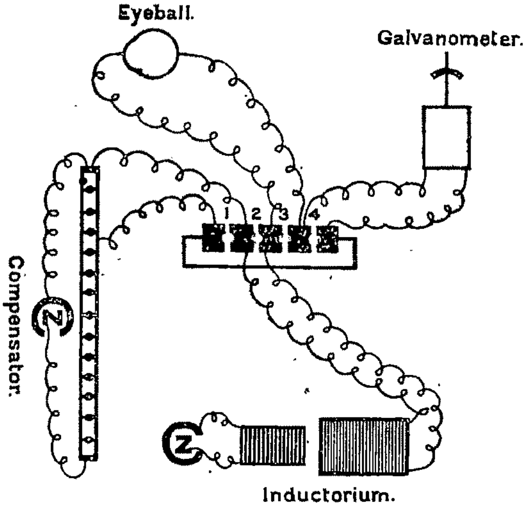
No. 3*b*.—"Four Observations concerning the Electrical Effects of Light upon Green Leaves."—*Proceedings Physiological Soc.*, 1900, June 30.

No. 4.—"Le Dernier Signe de Vie."—*C. R. Acad. des Sciences*, 1900, September 3.

In a previous communication (No 1) to the Society, a summary description of the electrical effects of light upon the eye was given; evidence was offered of their duplex nature, and their modifications were systematically considered.

The whole subject is more fully studied and described in No. 2, which contains at p. 32 the first mention of a phenomenon that I have designated as the "retinal blaze."

First experiment. (Demonstration on eyeball.)



PLAN OF APPARATUS.

This "retinal blaze" is a large electrical after-effect of a single electrical stimulus, and *in the same direction as that stimulus.*

Its modifications with physiological modifications of the eye. Its disappearance at death.

Sensitiveness to light is a chief property of the retina (and skin) of animals and of the green leaves of plants. Electrical effects provoked by illumination of green leaves were therefore sought for and studied. A preliminary account of the results is contained in papers Nos. 3*a* and 3*b*. An electrical response to light is witnessed only in the case of actively-living green leaves; it is absent from other vegetable tissues (coloured petals, fruits, seeds, &c.).

The electrical response of a green leaf to illumination is one of its signs of life. A petal or a seed does not exhibit this sign, and we must have recourse to some other test by which to distinguish whether it is alive or dead.

Such a test is afforded by a reaction similar in principle to that of "retinal blaze." The reaction is of a most general character, and indicates whether an organ or tissue, animal or vegetable, is living or non-living. It is the last sign of life (No. 4).

Second experiment. (Demonstration: Living *versus* dead nerve.)

Third experiment. (Demonstration: Living *versus* dead egg.)
Probable nature of the phenomenon. A post-anodic action current.

Mr. VICTOR HORSLEY—

(1) A lantern demonstration on the course of the fillet fibres in the cat.

(2) A communication with reference to the cat shown at a previous meeting in which Brown-Sequard fits had been obtained after a lesion of the medulla. Since that meeting Mr. Horsley had completely divided the mesencephalon, and the fits could still be obtained. The cat had been killed and photographs were shown to demonstrate that, except for a trivial involvement of the cerebellum, the initial lesion was confined to the medulla, and that in the second experiment the division of the mesencephalon had been complete.

BRAIN.

PART IV., 1900.

Original Articles and Clinical Cases.

HUGHLINGS JACKSON AND THE CORTICAL MOTOR CENTRES IN THE LIGHT OF PHYSIOLOGICAL RESEARCH.

BY PROFESSOR EDUARD HITZIG, M.D.

GENTLEMEN,—I am well aware that Horace of old has sometimes been accused of vanity for his ode "Exegi monumentum ære perennius." The poetical form, however, of the thought that pervaded the ode was perhaps only the expression of an antique simplicity; for the prophetic words of the same ode, "non omnis moriar," point to the fulfilment of a wish that pervades the breast of almost everyone. Nevertheless this hope of an existence reaching beyond what is in the more narrow sense mortal, has assumed a very different shape among various nations and religions and again among various professions and persons. One of the happy thoughts in this direction and one that first took a practical form in this country, aimed at preserving vividly and imperishably the memory of the mental achievements by which important men in our department elevated themselves above the great mass. The idea is to secure at stated intervals lectures upon some division of the science to which those men had devoted their best strength. Such a custom is in fact far more lasting than lifeless bronze and far better suited to the recognition of mental work.

We live in Time and it is therefore not vouchsafed to us to create anything absolutely imperishable. No one can say whether or not the intellectual monument which this society intends to erect to Dr. Hughlings Jackson—the honoured man whom we still to our joy number as one of us—will be of such duration as the poet prophesied for his work: "As long as the Pontifex ascends to the Capitol with the silent virgin." If, however, it be permitted to judge by the development which this society has shown in the fourteen years of its existence, by the amount of intellectual labour that its members have performed, and by the influence that these labours have had upon the scientific views of the medical and philosophical world,—then this monument will have a long life, and so long as it endures, so long will it offer to the illustrious scholar the most worthy of all rewards: His thoughts will ever again rise from the seemingly lifeless dust, and will spur posterity on to renewed intellectual labour in the field that he cultivated.

If we examine carefully the most important efforts in the realm of the natural sciences, we find that two qualities have always been especially effective: keenness of observation and curbing the imagination. The first quality is far less an attribute of the senses than it is of association. Hundreds see the same event without its exciting any thought. One single person, however, sees this event and he sees it with other eyes, because it connects itself in his mind with numerous other conceptions, and forms with them a whole which the imagination at once portrays as completed truth. Precisely here at the very side of this special pre-eminence of the inquiring mind, lies the danger. We learn the truth only when we stay upon the basis of reality, and when we prune back the luxurious shoots of the imagination, however they may for the moment please our inward eye. This is the ever renewed struggle *with* the hypothesis and *against* the hypothesis. It is not every inquirer that has been alike fortunate on every occasion in this struggle, as well as in general in the exercise of those two qualities. On the contrary we couple with almost every distinguished name the memory of some *one* particularly eminent scientific achievement. As for Dr. Hughlings Jackson there is no doubt that his merits are of the most manifold character, and there is further no doubt that for English physicians his personality has not failed to be of influence upon the estimate made of his work. But in foreign countries we connect his name above all with the memory of one fact, namely, that he was the first one who referred the partial cortical convulsions to peculiar centres of innervation. Many another had already observed these convulsions, but he alone hit the right explanation for the phenomena, and, by referring the convulsions to such centres, he argued the existence of motor centres in the brain, and even told to a certain degree about what their position was, before physiological research was able with certainty to prove where they were. The scientific world has therefore, as you all know, given to these convulsions the name "Jackson's convulsions." Under these circumstances, whatever part of Dr. Jackson's work later lecturers on this foundation may choose as the point of departure for their observations, it may well seem justifiable, nay imperative for me, the first one called upon for an estimate of his labours, to choose the subject:

What development, in consequence of physiological researches, has the doctrine of the cortical motor centres experienced since those investigations of Dr. Jackson's.

I think that in this way I shall meet the wishes of this society. For when it summoned me to be the first of these lecturers, it doubtless did so for no other reason than because I was precisely the first one, now some thirty and more years ago, to confirm by *physiological experiment* and to define more closely that which Hughlings Jackson had concluded from *clinical* facts. I hope and I believe that the members present, in consideration of my connection with these researches, will deal leniently with all such defects of this lecture as may arise from my imperfect command of the English language.

The character of the task set me requires that its solution be sought in the main by way of history. As a necessary consequence, part of this lecture will offer to some of the members only what is well known to them, and will certainly offer to many members at least much that is familiar. Still it may perhaps not be uninteresting to consider all these facts in a brief summary and to glance at them from the point of view from which they present themselves to a man who has for a long time occupied himself with them and with the questions associated with them. The material has in the course of these thirty years assumed very extraordinary proportions, and regard to time and to the occasion compels me to limit myself to those facts and to that part of the consideration of the facts which may be necessary to a clear, even if sketch-like, portrayal of the picture which we have to reproduce. I shall therefore be compelled to pass over numerous valuable contributions of English and other authors, even in the field of physiology, and to leave altogether to my successors in this office the consideration of the anatomical and pathological sides of these questions. In spite of this limitation it will at once be apparent that it is quite impossible to confine our view merely to the centrifugal functions of the cortical motor centres, and that we must needs, although only within certain bounds, busy ourselves also with the sensory functions of the brain.

The theme that is set before us points of itself to the proper beginning for our discussion. We have first to present the opinions which *Hughlings Jackson* uttered before the publication of the first physiological work on the cortical motor centres. Happily we have an article of his, termed "Study of Convulsions," in which he summed up these views of his immediately before the appearance of that work in the year 1870.

It will be best to proceed from Dr. Jackson's conception of the qualities of the brain substance. In reference to it he utters first of all with full decision the opinion that the gray matter and it alone has the property of starting motions, and in particular convulsions, a sentence that has ever been and ever remains for me an axiom. It is further his opinion that paralysis is produced by lesion of nerve fibres, a sentence the correctness of which, in this exclusive form, is open to objection. The genesis of motion from the gray matter is mediated by the contractions of the arterial vessels, and that in such a way that every antecedent utterance of activity on the part of a certain district of the gray matter excites by means of the arterial innervation the activity of another district. We may then consider these processes as discharges which spread themselves out in the gray matter according to the manner of the distribution of its blood-vessels. And if we accept this conception, then on the one hand the processes in breathing, in walking, and in thinking will be in principle the same, and on the other hand we shall not need to grant a qualitative difference but only a quantitative one between the violent and irregular motions of the cerebral convulsions and the co-ordinated motions of normal life which are effected at a small expense of power.[1]

We have thus defined these motions as a united whole and have found that they depend upon the presence of the gray matter. It follows from this that the relative amount of the gray matter favours the production both of normal and of convulsive motions. Therefore the corpus striatum, in so far as it contains a less amount of gray matter, will be less easily, and the cortex, in so far as it contains a greater amount of gray matter, will be more easily, qualified to produce all these phenomena of motion. Indeed, Jackson presupposes that the latter are "to blame in severe convulsions at all events."

The relation of the cerebrum to the corpus striatum is to be conceived of in such a way that in the latter the more simple and in the former the more intricate co-ordinations of impressions and motions in time and space are represented. In the former numerous other elements come into play, whereas at every point of the brain-cortex the units again appear which are present in the corpus striatum. Experience teaches that the motor functions of a whole half of the body can be annulled by the destruction of a small portion of the corpus striatum, whereas a far greater destruction of cortex does not lead to paralysis. Now this is based precisely upon that growth of new formations of nerve substance, by which those aggregates of the corpus striatum are in the cortex pressed apart over broad surfaces. We must not, however, picture to ourselves the structure of the nervous system as if in one convolution only the motions of the arm, in another only the motions of speech, and in a third only the motions of the leg were represented. On the contrary, each separate convolution contains a multitude of elements of one unit of the corpus striatum, for example, of the arm, and a smaller number of elements of another of those units, for example, of the leg and of the face.

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[1] This course of thought occurs often in numerous articles of Jacksons, for example, "Localisation of Movements," 1875, p. 33: "The inference is irresistible that there must be a motor as well as a sensory element in the 'organ of mind' which is faintly discharged when we 'think' of an object." "Slight discharges arise in the case of reproduction, strong discharges in the case of first production of sensible perception." "In the case of convulsions the discharge is excessive."

Taken as a whole the cerebral cortex is conceived of as an organ in which *motions and sensations* are represented, and in which there exists a definite kind of localisation for these motions and sensations, something after the manner in which Luciani conceived of them in one of his later works.

It is true that we learn but little here touching the part that the impressions on the lower and on the higher senses play in the cerebrum. Hughlings Jackson assumes that there is a certain segmentary connection of motor and sensory fibres with the corpus striatum, in so far as muscle nerves and the sensory fibres from the skin which covers these muscles meet there. He thinks that in this way it is possible to explain the interruption of the convulsion by the ligature of a limb. But he does not think that these bundles of fibres go as far as the cortex. As for the higher senses, we learn even, "that mere destruction of large parts of the hemisphere does not cause blindness, nor even defect of sight."[1]

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[1] On this point we find in "The Localisation of Movements," p. 41, the following statements: "I wish to point out that I have suggested that disease of the posterior lobes, chiefly of the right one, although it does not produce loss of sight, does produce loss or defect of visual perception (imperception); or as I now prefer to say, defect of recognition." (Who is not reminded by this of Munk's soul-blindness?) Further, in a note at the same place: "I make four statements (1) Destruction of no part of the cerebral hemisphere produces loss of sight. (2) Discharges of parts of it (I think posterior part chiefly) produce coloured vision. (3) Tumour in it leads to changes in the optic nerve (optic neuritis), in consequence of which defect or loss of sight may or may not follow. (4) Disease of the posterior lobe (right) produces defect of perception."

If we then consider the way in which Hughlings Jackson speaks of the motor functions of the cortex as endowed with the qualities that we have described, the conviction at once forces itself upon us that in all his considerations and conclusions he was impeded and misled by the firmly rooted error of that day, one based upon the doctrine of Flourens, namely, that the actual motor centres lay only and exclusively in the corpus striatum. We can follow him and see how Hughlings Jackson's own experiences and conclusions constantly kept forcing him back to the cortex, and yet at the same time that he was fettered to the corpus striatum, because the universal opinion of research referred the cases of unilateral convulsions, which depended upon the destruction of routes of conduction that lay in the capsula interna, to centres that were supposed to lie in the gray matter of these ganglia.[1]

The next consequence of this conception of Hughlings Jackson's, in connection with his hypothesis as to the part played by the blood-vessels, is that he looks for the place from which the convulsions that he treats of issue, in the field that is fed by the arteria fossæ Sylvii, seeing that this artery supplies the corpus striatum and many neighbouring convolutions with blood. The very important utterances about the clinical symptoms that accompany aphasia agree with this conception; for an attack of convulsions that brings in its course a temporary loss of speech, always begins on the right side in the face or in the tongue, and no such defect of speech occurs when a similar attack begins in the right hand or in the right foot. Dr. Jackson says decidedly that the only conclusion he can draw is that the illness, on which that loss of speech depends, sits chiefly in that part of the corpus striatum which includes Broca's convolution, and in the same way that the *hemiplegia* that appears after such attacks is dependent upon changes in this region. Hughlings Jackson likewise states as a result of his experience, that convulsive attacks which show tumour symptoms and which begin in the hand depend upon a lesion of convolutions of the arteria fossæ Sylvii. The suggestion that the cause of a convulsive attack that begins in the foot is perhaps to be sought in the neighbourhood of the thalamus opticus is less fortunate.

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[1] Compare "Localisation of Movements," p. 2: "At that time [1868] however, I believed the corpus striatum to be the part discharged in *convulsions* beginning unilaterally, although then and several years before I believed the convolutions also to contain processes representing movements."

We have already seen that the cortex played in fact essentially no other part in Hughlings Jackson's view at that time of the case lying before us, than the further central gray matter. It must be capable of producing and storing great quantities of material for discharges or for explosions. And it was then necessary that this material, either constantly or in single attacks, should be discharged through all the lower centres by the use of the motor tracts. General epileptic convulsions and the convulsions named after Dr. Jackson differ from each other only in the one particular, namely, that the latter arise from discharges in convolutions which lie farther from the motor tract, whereas in the common epileptic attacks the discharges are in convolutions nearer that region. The influence of the cortex upon movement only goes as far as that. Todd's epileptic hemiplegia in particular, does not depend directly upon organic unsoundness; it is the result of overwork of the nerve fibres which lead from the discharging part to the convulsing muscles.[1]

It is well known that one of the most important services rendered to science by Dr. Jackson consists in the description of the way in which these partial attacks of convulsions of his develop. He says in this passage: "Fits which begin in the foot have a different march from those which begin in the hand. When a fit begins in the hand it goes *up* the arm and *down* the leg. Now patients who have fits beginning in the foot tell me that the spasm goes *up* the leg and *down* the arm."

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[1] "Disease in the hemisphere never causes palsy limited to one side, unless it also involves or squeezes the motor tract. . . . It does not cause hemiplegia, that is, by *destroying* a large part of the hemisphere. . . . The palsy depends upon secondary changes near the coarse disease, or rather on the 'overwork' of nerve fibres by the excessive discharge on them which these secondary changes permit. . . . The assertion is, that hemiplegia does not result from the *lack* of the part of the hemisphere *destroyed* by the disease."

"The fit begins most often in the parts that suffer *most* in hemiplegia, and these are always the muscles which are most concerned in arbitrary, isolated motion."

There are few cases in which the fits begin elsewhere "than in the side of the face (usually in the cheek), in the hand or in the foot; they very rarely begin in the upper arm or in the calf. . . . Fits beginning in the hands are common, fits beginning in the cheek and tongue are less frequent, fits beginning in the foot are rare. . . . The fits which begin in the hand, begin usually in the index finger and thumb; fits which begin in the foot begin usually in the great toe."

If we consider the total result of these doctrines of Dr. Jackson, we shall easily recognise from our present point of view, in what places and in how many directions they still needed completion and correction. And at the same time we grasp the fact that on the one hand clinics, on the other hand physiology, and finally anatomy, while each has shown its own right to independent research, still are to such an extent dependent upon each other, that the full recognition of truth can only arise from the common application of the results of all these sciences.

It is probably scarcely possible to prove this more strikingly than by the influence which the very first physiological researches as to the qualities of the cortex exercised precisely upon the conclusions drawn from those clinic and anatomic observations, and especially upon the theories of Hughlings Jackson.

These experiments are so well known that I may waive a closer description of them and content myself merely with the emphasizing of a few points which are hereafter to be discussed.

It was proved by experimental excitation, using the galvanic and the faradic current, that the muscles of the extremities, of the neck, the trunk, and of those innervated by the facial nerve, could be set in motion from certain narrowly bounded places of the gyrus sigmoides and of a neighbouring convolution in the brain of the dog. It was further discovered that the removal of very small portions of the surface of the cortex of the gyrus sigmoides produced a peculiar disturbance of the motions. And, finally, Dr. Jackson's theory touching the charging of the cortex and its discharge in local and in general fits of convulsions, found a practical confirmation by the method of the Faradic excitation. As a matter of fact the cortex, and that even by a short series of merely weak inductive shocks, can be so charged that even after the stimulus has ceased local fits of convulsions arise, which may spread further and develop into general fits. *The phenomena of such a charging* have been more thoroughly examined and graphically presented by François-Franck and Pitres. A charging of this kind can be effected from more distantly existent points of the cortex, and for this reason the electric examination of the cortex should never be attempted without the control with the galvanic current, which does not lead to a residual charging of the cortex, or should only be attempted with single inductive shocks.

The way in which this discharge spreads out was described in general lines by the first discoverers themselves. The later researches of Luciani,[1] Franck and Pitres,[2] Unverricht,[3] and many others, showed in agreement with them that the stimulus imparts itself from the originally excited point to the neighbouring cortical regions. In particular, Luciani first of all, and then Munk,[4] Bubnoff and Heidenhain,[5] Ziehen[6] and others, showed that by the removal of a locally limited portion of the cortex such a discharge could be influenced to such an extent that the motors represented in the parts removed no longer convulsed in the former manner. Chiefly by pursuing such artificially excited fits of convulsions on the brain cortex of apes and comparing them with the monospastic and hemispastic fits, which were now better understood, it was discovered that all these facts agreed with each other and with the exemplary clinical description given of them by Hughlings Jackson. This comparison showed, however, at the same time, that the hypothesis set up by him was only correct in so far as it referred to the existence of cortical centres in general, but not in so far as concerned the assumption of manifold centres by means of which the different courses of these fits of convulsions were to be explained.

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[1] LUCIANI, "Sulla patogenesi dell' epilessia." *Rivista sperim. di freniatria,* 1878 and 1881.

[2] FRANCK and PITRES, "Encephal." *Dictionn. encyclop.* (Dechambre).

[3] UNVERRICHT, "Experimentelle und klinische Untersuchungen über die Epilepsie," *Arch. f. Psychiatrie,* Bd. xi.

[4] MUNK, *Lehrbuch der Gehirnkrankheiten von Wernicke,* 1881, Band i., S. 240.

[5] BUBNOFF and HEIDENHAIN, "Ueber Erregungs und Hemmungsvorgänge innerhalb der motorischen Rindencentren," *Pflüger's Arch.,* Bd. xxvi.

[6] ZIEHEN, "Ueber die Krämpfe infolge elektrischer Reizung der Grosshirnrinde," *Archiv. für Psych.,* Bd. xiii.

Little, however, as we could enter into the particulars of the researches which we first mentioned, just as little can we go into the details of the extremely numerous researches by means of which the facts we have just mentioned were rounded out. My task is rather to discuss the various theories according to which the newly-found facts were conceived and explained.

We may divide the questions here raised into two unequal groups, namely: (1) *The question whether the sum total of our experience justifies the assumption of centres in the brain cortex, and* (2) *the question which has received such extremely different answers, in what way such centres may be supposed to act.*

It would, of course, be the right thing to define at the very outset of this discussion, what is to be understood by the notion "centre," and all the more right because this expression has been applied in the literature in the most different ways and has given rise to disagreeable misunderstandings. But it will soon appear that no such universally valid definition can be given in a few words. Nevertheless we may content ourselves for the needs of the moment by understanding that a centre is a locality in the brain cortex, not bounded by lines, within which certain groups of conceptions are anatomically and functionally localised. In the case before us it would then be a matter of ideas of motion and of motor functions without any respect to the way in which we suppose them to have originated. The essential point is therefore the validity of the localisation, or in other words the question as to whether the doctrine of Flourens with reference to mobility be still tenable or not.

The existence of such centres has always been and still is contested by Goltz and a number of his pupils, by Schiff and others. These opponents raised a series of objections to the force of the evidence of the experiments both in stimulus and in paralysis.

As for the former, Goltz[1] especially, among many others, has renewedly declared that they proved nothing at all in the face of the possibility of the diffusion of the electrical current. But he has never taken up my challenge to show me the place at which these currents could with any real effect diffuse, and he has finally given us to understand that he probably means the layer of fibres lying directly under the cortex. Moreover, the question was discussed with the greatest caution even in my first article. At that time, arguing on the one hand from the direct cortical excitation, and on the other hand from the excitation of the white matter by isolated needles, I had concluded that only the excitability of the latter had been directly proved, but that we could indirectly conclude at least the function if not the excitability of the gray matter in so far as under the circumstances we were of necessity forced to assume that those excitable fibres had their origin in the neighbouring cortical cells.

Since that time, however, the direct proof of the electrical excitability of the cortex, of the existence of centres in it, and the direct confirmatory proof against the objections raised, has been brought out in the most manifold way. It was found that after the undercutting of the cortex the electric stimulus only took effect in case an extraordinarily strong current was applied, but that neither the cutting around a centre, which did not hinder the diffusion of the current, nor its isolation by means of glass plates, which did hinder the diffusion, changed in any way the effects of the electrical stimulus, provided only that the direct cortico-muscular path remained uninjured. And the experiments of Bubnoff and Heidenhain,[1] and as well those of François-Franck and Pitres,[2] were absolutely decisive; they proved that the gray and the white matter had a totally different kind of electrical reaction. The time of reaction, the time between the entrance of the current and the beginning of the twitching, is materially shorter in the case of excitation of the white matter than in that of the gray matter. The muscle curves, drawn in each, show the most essential differences from each other; and finally the white matter does not possess the power of being charged by inductive currents and of then discharging itself in local or general convulsions. A similar testimony is to be found in the different reaction of the cortex and of the marrow upon a number of poisons.

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[1] FRIEDRICH GOLTZ, "Ueber die Verrichtungen des Grosshirns," *Gesammelte Abhandlungen*, Bonn, 1881.

The interesting experiments of Horsley and Gotch[3] proved further that a negative variation (Du Bois-Reymond) of the current of the resting nerve in the spinal cord occurred when the corresponding cortex centre was excited, and only when precisely this centre was excited. Finally, within the last few months Larionow's[4] experiments have taught us that this negative variation can also be traced in the reverse direction, in so far, namely, that the currents of cortical action experience a locally limited change when peripheric stimulus is applied.

If we put all these facts together there is not room for the least doubt that even from the results of the different methods of electrical experiment alone, the existence of functionally different centres, especially of such as are of a motor character, in the brain cortex itself, would be made sure even if the results of the experiments in extirpation did not speak in the same sense.

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[1] BUBNOFF and HEIDENHAIN, "Ueber Erregungs und Hemmungsvorgänge innerhalb der motorischen Rindencentren," *Pflüger's Arch.*, Bd. xxvi.

[2] FRANCK and PITRES, "Encephale," *Dictionn. encyclop.* (Dechambre).

[3] HORSLEY and GOTCH, "On the Mammalian Nervous System," &c., *Philosoph. Trans.*, vol. clxxxii., 1891.

[4] LARIONOW: "Ueber galvanometrische Messungen der Ströme in der Rinde der Schläfenwindungen bei Reizung der peripheren Gehörorgane," *Monatsschr. f. Psychiatrie*, &c., Bd. v., 1889, S. 464. A more detailed publication than that in the passage cited, will perhaps dissipate many a doubt as to the author's results. I have occupied myself with similar experiments since the year 1874.

It is true that Goltz, whom we may doubtless regard as the representative of the opponents of the doctrine of localisation, has until of late contested this doctrine most zealously by his experiments in extirpation. We shall, however, see that his own experiments, in spite of all he may say against it, have really, nevertheless, although by a very roundabout way, led him back in the main to the very same mode of viewing the case that formed as long ago as the year 1870 the point of departure for my consideration of the functions of the cerebrum. I have always valued and recognised in the highest degree Goltz's services in the field of the physiology of the central nervous system. If he has in spite of that given occasion to unpleasant conflicts and thereby also to the spreading of great confusion over the questions with which we are busied, it is perfectly clear, for every one acquainted with the literature, that the reason for this lies in the unsuitable method of operation which he used at the beginning of his experiments. The moment that he applied methods which permitted, even if it was only an imperfect localisation, he reached results which it is quite possible to harmonise with mine and with those of scholars who think as I do.

It is well known that Goltz began his extirpations by flushing the matter of the brain with a jet of water which he brought to bear on the brain by means of variously shaped pipes after trepanning in one or more places. In this way he flushed the brain in the most different directions and in different depths, without telling what was the extent of the injury caused, and without, in my opinion, being able to control that extent. He himself alleges that by this process, by a pressure on the oblongata, in the case of very many animals there occurred a sudden cessation of breathing and of the pulse. In the case of other animals he mangled the brain with an instrument proposed by R. Ewald, a so-called scissors-borer.

If we wish to make experiments in *localisation*, it is —however much Goltz may have said or may say against it—a simple demand of logic that we either bring stimulus to bear or cause lesion *locally*, and that we then compare with each other the phenomena produced in this way at the different places of the surface or of the interior of the brain. The methods that Goltz at that time applied were, however, clearly not suited to investigate the qualities of fixed localities of the cerebrum, in so far as these methods purposely injured large parts of it and extended unintentionally their effects far beyond the cerebrum, even as far as the medulla oblongata. Even though it is beyond doubt that in this way many a valuable bit of knowledge about the functions of the brain was attainable, no one can be surprised that Goltz at first came to the conclusion that not the *place* of the loss of substance, but only its *amount*, had a decisive influence upon the character of the disturbances. That was so clear to him that he even says in so many words: "In the subsequent statements I may therefore as a rule omit a sufficiently exact designation of the place of the lesions."

But the moment that Goltz applies methods, which, although still far from meeting the demands made by me, nevertheless no longer attack the whole cerebrum, but rather either its anterior or its posterior half, he finds, certainly to the surprise of his readers, that he is compelled to make, word for word, the following remark: "I read in different authors with the greatest astonishment the observation that I had declared that the matter of the brain is everywhere of like value."[1] When then Goltz in his sixth article also repeats the sentence, that he holds the assumption of small limited centres as more nonsensical than ever, he is still forced in the same article to concede that as a consequence of mutilation of the *anterior* half of the cerebrum, all motions become coarse and awkward, while in another passage he concedes that the dog operated upon *behind* moves all the muscles of his body with normal skill, has undisturbed sensation of touch, does not step into the air, and shows no increase of reflex excitability, but that on the other hand it suffers chiefly, though not exclusively, from disturbance of vision. Had Goltz taken a still further step in the limitation of his operative lesions, he would surely also have seen a further limitation of the consequences of his operations, that is, a clearer localisation. I may refer here to my lately published experiments,[1] which prove the exceedingly great sensibility of the brain even towards apparently indifferent operations. It has become clear thereby that the mere uncovering of the brain to a slight extent, without lesion of its matter, may lead to evident disturbances of mobility, of sensibility, and of the power of vision. How can anyone then be surprised that the most manifold disturbances of functions should appear, if he opens the skull to a large extent and makes the greatest inroads upon the brain? Thus far Goltz has constantly evaded my challenge to compare the effects of the strictly localised lesions with each other. Another reason for misunderstandings I shall mention later.

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[1] Goltz, "Ueber die Verrichtungen des Grosshirns, Fünfte Abhandlung," *Pflüger's Archiv.*, Band xxxiv.

Luciani's[2] doctrine stands in very close relation to these explanations. This scholar, whom I highly respect, reached, as is well known on the basis of his experiments, the view that the single centres overlap each other, and that in consequence, although every function can be injured the most from a certain central region, at the same time a number of other functions are also in a greater or less degree injured with it. This agrees with the above-mentioned view of Hughlings Jackson that in every gyrus a larger quantity of the one function and a smaller quantity of various other functions are represented. A peculiarity of Luciani's doctrine is the construction of a "centre of centres," which he places in the neighbourhood of what I call the centre of the facial nerve. At that point he thinks that all the rest of the centres, the one overlapping the other, are interwoven with each other, so that by an injury to this central centre the most severe psychical disturbances and the most complicated results are produced. Luciani ascribes a very special importance to this fact.

Nevertheless his whole doctrine, and in particular the last-mentioned fact, is incorrect. It is, indeed, incontestable and *a priori* necessary that the single cortical centres be connected with each other, so, for example, that every sensory centre must certainly be combined functionally with motor elements of consciousness. But this connection does not exist in the way that Luciani assumes and it cannot be proved by the method that he applied. For this purpose such large extirpations as he practised are useless. If the mere uncovering of a narrowly limited cortical field occasions clearly appreciable disturbances of this whole field, and even changes in its neighbourhood, it is plain that severe lesions in large cortical fields must much more certainly lead to manifold disturbances of the functions of the neighbourhood, and thus Luciani's results are to be explained. For the purpose that he had in view he should have applied both the method of the very least excitation and the method of the very least lesions. A single experiment of this kind proves the falsity of Luciani's whole doctrine. If, for example, we set a small trepanning bit at the place that corresponds to his centre of centres, and if we then cause a small or even a somewhat larger lesion at this point, but at the same time see to it that the wound heals aseptically, this operation remains, in very many cases, without visible influence upon the functions of the animal operated upon. Eckhard[1] reached, in this respect, the same results that I myself reached. Now a very much smaller lesion of the gyrus sigmoides produces severe disorder in the functions of the extremities and of the eye, therefore we should look for much more severe phenomena in the case of the lesion of so important an organ as the centre of centres. Luciani's error is simply to be explained by the fact that the so often mentioned locality lies about in the middle of the convexity of the brain, so that a coarse attack upon it is precisely best fitted to make all the rest of the convexity suffer with it.

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[1] E. HITZIG. "Ueber das corticale Scheu des Hundes," *Archiv. f. Psych.*, Band xxxiii., Heft 3.

[2] LUCIANI and SEPPILLI, *Die Functions—Localisation auf der Grosshirnrinde*, 1886; and "On the Sensorial Localisations," &c., BRAIN, July, 1884.

If we draw the sum total of all these experiences, we find that the paralysing experiments speak in the same way as the excitation experiments, in other words, that all experiments, in so far as they are entered upon with the necessary precautions, prove the existence of centres in the cortex, and that in so far as they are entered upon without such precautions, they have produced no facts that would be inconsistent with the cortical localisation.

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[1] ECKHART, C. "Das sogenannte Rindenfeld des Facialis in seiner Beziehung zu den Blinzbewegungen." *Centralblatt f. Phys.*, Bd. xii., Nr. 1.

If we now turn to the second of the questions set before us—*the question as to the functions of these centres*—we must proceed from the description of the facts which their first discoverers were able to observe as a consequence of very small extirpations, and which, in the main, so far as the motor side is concerned, retain the same appearance in the case of large lesions.

These experiments showed that such lesions in the case of a dog never produce an actual paralysis in the form in which it appears in men, and in fact that, as later experiments showed, this was not even the case when the operation was on both sides and symmetrical. On the other hand, the extremities reached a condition which we defined as showing *that the animals operated upon had but a defective consciousness of the condition of their limbs, and that they had lost the power of forming for themselves complete conceptions as to these limbs.* This condition displayed itself chiefly in that the animals used their limbs actively in the most unsuitable way, and that they did not correct the most unsuitable positions which were passively given to their limbs.

These facts have been enlarged in the most manifold manner in the thirty years that have passed since that time. Inasmuch as the same experiments were also extended to other species of animals, the consequences of similar experiments differed more or less, doubtless, from the consequences shown by the experiment on the dog. But none of the further experiments have in the least changed any of the actual results that we reached then by the conduct of the dogs upon which we operated.

The enlargement of our knowledge has, however, led to a series of different theories as to the significance of those centres. The chief theories are: (1) The motor theory; and (2) the sensory theory.

The principal representative of the motor theory is D.

Ferrier,[1] a scholar to whom, as all know, the physiology of the brain owes, among other things, the discovery of a number of new facts in the realm of the excitation experiments. In the question now under consideration he proceeded from paralysis experiments, which he made in the motor region of apes. He reached therein, we use his own words, the following conclusions: "That the thus produced affection is a purely motor one, and the centres or regions in question are strictly motor, but motor in a special or limited sense, viz., psychomotor,"[2] and that "strictly cortical lesions of the motor area do not cause anæsthesia in any form, and it may be laid down as a rule, to which there are no exceptions, that if anæsthesia is found along with motor paralysis, the lesion is not limited to the motor zone."[3] "Though an animal does not react so readily to sensory stimulation of the paralysed side, it does not follow that this is due to diminished or absent perception of the stimulus. An animal may not react or react less energetically to a sensory stimulus, not because it does not feel it the less, but because it is unable, or less able, to do so from motor defect."[4]

Ferrier declares in this way most decidedly that sensory disturbances are lacking, while other authors, and among them especially Munk[5] and Mott,[6] and of late also Bechterew,[7] declare in just as decided a manner that they are present. Besides, even Ferrier has a short time ago in co-operation with Turner[8] in large experiments of extirpation found hemianæsthesia combined with hemiopia. But all these symptoms are explained by the latter author "by a dynamic influence exerted by the magnitude of the lesion on the sensory centres or tracts which were not organically injured." "This explanation receives support from the fact that in smaller cerebral lesion—for example after the removal of the so-called 'leg area' alone—no such symptoms occurred."[1]

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[1] D. FERRIER, "The Functions of the Brain," second edition, 1886.

[2] *Ibid.*, p. 362.

[3] *Ibid.*, p. 378.

[4] *Ibid.*, pp. 374, 375.

[5] MUNK, "Ueber die Functionen der Grosshirnrinde," 2 Aufl., 1890; and "Ueber die Fühlsphären der Grosshirnrinde." Sitzungsberichte der Akademie der Wissensch., 1892-1896.

[6] FREDERICK W. MOTT, "The Sensory function of the Central Convolutions of the Cerebral Cortex," *Journal of Physiology*, vol. xv., 1893.

[7] BECHTEREW, "Ueber corticale Centren beim Affen, *Neurologisches Centralblatt*, 1898, p. 140.

[8] FERRIER and TURNER, "An Experimental Research," &c., *Philos. Transactions*, vol. cxc. B., 1898, pp. 1-44.

Finally, a very short time ago Schäfer[2] has come over altogether to Ferrier's side, in so far as he states that apes, after larger or smaller extirpations in the motor zone, still felt the slightest touch of a straw, &c. According to him "it cannot therefore be the case that the motor paralysis which is produced by a lesion of the Rolandic area is due to a sensory disturbance. And it also follows that tactile sensibility is not localised in the same part of the cortex from which voluntary motor impulses directly emanate."[3] We perceive that we have here astonishing differences of opinion as to observations of what is purely matter of fact, such differences as in other cases scarcely occur in reference to explanations.

My own experience as to the ape does not put me in a position to pass a judgment of my own in this question. I can only do this by way of conjecture, and by using the further literature as well as the experience I have had as to the dog and as to man. But even with reference to the dog, Ferrier speaks no less decidedly. He declares that the sensibility is not injured by lesions in the motor zone even of these animals, and says in so many words: "It is inconceivable that brains constructed on the same anatomical type, should differ fundamentally in their physiological organisation, and we may well assume that, however much the facts of experiment on the motor centres of dogs may appear opposed to those of monkeys, they are not so in reality ![4]

If we remember one of those theses of Hughlings Jackson, that the single elements of the subcortical centres in the cortex are pressed farther apart by the intrusion of other organisations, we can concede the last sentence, but, as we shall still see, without reaching the same conclusion as Ferrier.

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[1] FERRIER and TURNER, "An Experimental Research," &c., *Philos. Transactions*, vol. cxc. B., 1898, p. 36.

[2] A. SCHÄFER, "On the Alleged Sensory Functions of the Motor Cortex Cerebri, *Journal of Physiology*, vol. xxii., No. 4, Nov. 25, 1898.

[3] *Ibid.*, vol. xxii., p. 312.

[4] D. FERRIER, "The Functions of the Brain," p. 361.

It can under no circumstances be in any way doubted that any lesions at all in the motor part of the gyrus sigmoides of the dog are always and without exception combined with disturbances which affect the sensibility of the whole limb, that is to say, of the skin, of the muscles, of the joints, &c., and that these disturbances can in no case be an illusion caused by purely motor disturbances, or, more correctly expressed, by a "motor defect." In this reference to a matter of fact I agree with Schiff, Goltz, Munk, and the others, that is to say, with authors whose views I in other respects most decidedly oppose. If, then, Ferrier is of another opinion on this point, that can only be based upon the circumstance that he has not yet fully enough studied these "motor disturbances" of the dog.

Since the dog then undoubtedly shows disturbances of his sensory functions as a consequence of those lesions, it appears to me to be *a priori* impossible, or to speak with Ferrier, it would be "incomprehensible" if such disturbances were not to be observed in the ape. The reasons why they have escaped individual observers may be of a manifold description. They may, for example, depend upon the differences in the extent and depth of the lesion; this would agree with the fact that Ferrier and Turner found hemianæsthesia in the case of great extirpations, whereas Ferrier alone, in what appear to have been smaller extirpations, did not find hemianæsthesia. On the other hand, we cannot deny the correctness of Schäfer's conclusions, when this distinguished scholar, after he had found the sensibility intact in the palsied limb of the ape, says that the motor paralysis could not possibly be based on a totally imperceptible sensory disturbance. However, I shall have to return to this question in discussing Munk's doctrine.

The theory according to which the disturbances mentioned, and therefore also the normal motor actions, are to be referred to disturbances of the sensory functions, has been very differently expressed by different authors.

The first one whom we have to name here is Schiff,[1] to whom, aside from the discovery of many other important facts, we owe the discovery of the cortical sensory disturbances. To put it briefly, in almost all his works Schiff considers the disturbances of motion that are to be observed in dogs to be first of all the consequence of a disturbed sensation in the skin, of a disturbed sense of touch, but is not willing to have either one symptom or the other referred to the lesion of cortical centres. On the contrary, he denies the existence of such centres.

We can dispose very quickly of the series of proofs which he bases upon his explanation of the effects of electrical stimulus. For in the complete edition of his essays, although he formally declares that he still holds to his old opinion, he simply omits the plan chosen to demonstrate his theory and all the arguments based upon it, after I had proved to him its internal impossibility.

Nevertheless, he has not had much better luck in his considerations as to the results of the paralysing experiments. Ferrier, as we have seen, regarded the cortical disturbances of motion as purely motor and rejected any and every concurrence of sensibility, whereas Schiff asserts precisely the opposite, namely that the destruction of these centres produces no motor paralysis at all, but merely destroys the sensibility to touch and *therewith the consciousness of the position and situation of the limbs.* Schiff has at every opportunity accused me of changing my view as to the motor nature of those disturbances of motion, and has claimed that our views are no longer very far apart. This last may to a certain degree be the case, but the first is totally incorrect, since I never spoke of a purely motor function of these centres in the sense that Schiff attributes to me. I have from the very beginning and without any cessation, as I have just represented it, designated these disturbances as disturbances of the perceptive activity. On the other hand Schiff has himself in the course of the years changed his opinion in the greatest measure conceivable. For he has at last not merely reached the position that I have held from the first, but he has also in reference to the ape and with the aid of a number of considerations, which are altogether my own, with all decision expressed the view that *motor paralysis* can be produced by lesion of those cortical centres.

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[1] SCHIFF, *Gesammelte Abhandlungen.*

Schiff did, it is true, originally concede the existence of such centres in general, but he repeated over again that they could not lie in the cortex but must lie down below, and he heaped up proof after proof of this. Later he allowed this question to fall altogether out of the discussion. Originally, as we have said, he was only willing to deduce the disturbances of motion from a disturbance of the sensibility of touch. Later, however, he refers them to disturbances of the consciousness of the limbs and of the external parts of the body, that is to say, he explains them precisely as I do, and even citing my own words. And finally, Schiff has himself expressed the opinion that, as we ascend in the series of animals, centres advance from the subcortical regions even into the hemispheres, and this might in particular well be true of the centre of locomotion. In connection with this, from the fact that an ape does not grasp a fig which it clearly wishes to seize, he concludes that a paralysis is present similar to that of the hemiplegic man. Therefore, in his own words, a centre that mediates motion—a moving centre—must be injured. And if he had injured it by his operation, it must then be present at the place operated upon.

A more complete conversion than the one depicted is scarcely possible, for it goes very much beyond the measure that we observed when we treated of the successive works of Goltz.

Munk for his part assumed at the outset a totally different position. Whereas Schiff referred the disturbances of motion that were observed exclusively to the lesion of sensory ways in the cerebrum, and denied almost to the end the existence of cortical centres, Munk[1] on the contrary stood up from the beginning for the strictest localisation of the cortical functions and that to a degree which in certain respects goes far beyond my own views. On the other hand, he also refers the motor disturbances now under consideration to lesions in the sensory sphere, it is true more in appearance than in fact. I say "more in appearance," because he designated the parts that I called *partly* excitable[1] *partly* motor[2] region, by the name "independent spheres of feeling."

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[1] MUNK, *Ueber die Functionen der Grosshirnrinde*, 2. Aufl.

As a matter of fact Munk himself in his first communications named this section of the cortex a "motor sphere," and it was not until his third communication in the year 1878 that he used the name "sphere of feeling," supposing at the same time that he could thereby lead to a deeper understanding of this section of the cortex. He thought that he could compass this by localising all the feelings and the conceptions of feeling of each part of the body, that is to say of the skin, of the muscles, and the innervation feeling and conceptions of feeling, excluding, however, the common sensibility in the respective part of the sphere of feeling.[3] According to this we have to do in the sphere of feeling only with perceptions and conceptions which flow from the sensations of feelings, and therefore the conceptions of motion *alone* in the sphere of feeling are the causes of the so-called voluntary motions.[4] Correspondingly, lesions of these spheres produce according to their size the temporary or permanent loss of a part of, or of all, feeling and conceptions of feeling of the part of the body in question—psychical paralysis, or cortical paralysis of that part of the body.

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[1] A remark is here necessary against Ferrier. On page 225 of the second edition of his work, "The Functions of the Brain," he has thought it necessary to observe, against my word "excitable" that there is no reason to assume that any parts of the cortex are not excitable. This observation is a stroke into the air, for he will find that on page 19 of my book, "Untersuchungen über das Gehirn," in the footnote, I have defined the expression "unerregbar" (not excitable) in the following words: "We call here, without any prejudgment, all those parts 'not excitable' from which we can produce no twitchings."

[2] As for the expression "motor," I have repeatedly defined what I wish to be understood by this word, which I use for the sake of brevity. On page 65 of the work cited in the foregoing note, I protested, among other things, expressly against Mr. Ferrier's statement which makes me say that I had produced paralysis by experiments in extirpation.

[3] MUNK, *Ueber die Functionen der Grosshirnrinde*, 2. Aufl., p. 32 and pp. 38, 39.

[4] *Ibid.*, 2. Aufl., p. 48.

First of all we must contest some of this doctrine as not correct, or, at any rate, not proved. Even if it be correct—and that follows clearly enough from Schiff's experiments—that the *conceptions of feeling* are injured by lesions in these spheres, I see no proof advanced for the statement that this also holds good for *feeling*, at least so far as the cortex is directly concerned. Indeed, it is for *a priori* and experimental reasons very probable that all feeling is formed subcortically and that only its apperception as well as its endowing with local signs takes place in the cortex, and we must not forget that the emphasizing of the relations of the local signs to the cortex is one of Munk's services to our science. In so far then as an injury of feeling itself occurs, it is probably to be referred to a checking of the functions of the subcortical organs. Munk was finally compelled to concede this, although at first only in the sense that even the sensations of pain from the extremities arise in the opposite extremity regions,[1] whereas he had originally excluded their participation in those apperceptions. In so far then as the dog is concerned, there is at present not the least reason to doubt the doctrine *that in the extremity regions only the conscious working over of all the feelings that arise subcortically to more or less well localised conceptions of feeling takes place*. In the second place, it is not correct to say that all the parts of the sphere of feeling behave alike in the relations mentioned. Only a short time ago Eckhard[2] proved that "the cortex field of the orbicularis had no influence on the *reflex* activity of the subcortical centre for the motions of the eyelids."

And finally the theory as to the origin of the muscular motions from this "sphere of feeling" needs a limitation which we shall make in a moment; but, with this limitation, Munk's theory agrees so exactly with the theory that I myself suggested, that it is impossible to accede to his claim that he himself first showed the way to the due understanding of the functions of these regions. You will remember that I had defined in general the character of the disturbances mentioned " as disturbances of the consciousness of the extremities as well as of the power to form for oneself complete conceptions of them," and it will not have escaped you that in this general definition Munk's definition is contained so far as it is correct. Furthermore this definition leaves room for enlarging the latter at pleasure, an enlargement which I at a later date, and that with reference to certain disturbances that arise in case of lesion of the extremity region, disturbances in the influence of the objects of sight upon the movements of the animals, shaped as follows, namely, that in consequence of such lesions external circumstances—sometimes of the muscles (&c.), sometimes of the objects in space—are not taken into account by the sensorium for the movements of the limb affected, but only for these.[1] As for the rest I have in another essay touched upon the question—" whether the centre that is thus brought forward be the organ that alone rules the muscular movement in question, or whether there be still another motor organ within the same chain of action."[2] This question I answered in the sense that Munk later accepted, that 'I found the cause of the so-called voluntary movements not *only* in the conceptions of motion in the sphere of feeling, for this is not correct, but that I also beheld in them *one* of these causes and a necessary component of these motions. In fact the conceptions of motions *in themselves* lead only in a limited range of cases to movements, and in all other cases there is need of the intervention of another excitement of the senses or of an intellectual occurrence in order to disengage the conception of movement and therewith the act of motion.

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[1] MUNK, *Ueber die Fühlsphären der Grosshirnrinde*, Sitzungsber, I. Mitteilung, p. 31, 1892.

[2] ECKHARD, C., "Das sogenannte Rindenfeld des Facialis in seiner Beziehung zu den Blinzbewegungen," *Centralblatt f. Phys.* Bd. xii., No. 1.

Before I pass on to the presentation of my own view as to the nature of the functions of those centres, you will permit me to remind you that a glance at what I have already said teaches: (*a*) that the scholars who have occupied themselves most particularly with the experimental study of the brain, have finally, even if in part after long struggles, acknowledged, even if in different degrees, the differences of value in the cortex and therewith the localisation of the psychical functions in this organ;—(*b*) that all scholars without exception have come to the opinion that by lesion in what I call the motor zone the motions of the animals are impaired;—(*c*) but that there are differences of opinion as to whether only the motor functions or whether other functions also are injured, so that from this point again differences of opinion arise as to the reason for and the method of origin of the motor functions and of their disturbances; although these reasons are it is true sought by most authors, in agreement with the view expressed by me at the outset, in the conceptive activity or in a disturbance of the conceptive activity.

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[1] HITZIG, " Untersuchungen über das Gehirn," Neue Folge, *Reichert's und Du Bois-Reymond's Archiv.*, 1876, H. 5, S. 705.

[2] *Untersuchungen über das Gehirn*, 1874, p. 60ff.

If we follow up the further reasons for the differences of opinion which still obtain, we shall find that they consist in the main in two circumstances:

(1) In the fact that the knowledge won by a number of scholars touching various animals and man has been applied without sufficient respect to the anatomical and physiological differences of the brains of these species.

(2) In the fact that functions, which were more or less lost after such lesion, really or apparently return.

I shall reach the exposition of my own views most simply if I try to dispose of these difficulties, so far as that is possible in the present state of our knowledge, and if I therein start out again from the brain of the dog, the functions of which are best known to me from my own experiments.

The disturbances in motion, which follow upon lesion of the gyrus sigmoides of this animal, may be divided into various groups. We are well acquainted with the disturbances which I myself first described and which in the main consist in the circumstance that the dog, actively, brings his extremities into *abnormal positions*, and that it, passively, allows them without opposition to be brought into such positions. I myself at that time referred these peculiar phenomena to the lack of the conceptions which the normal dog forms of the condition of his organs of motion and especially of his muscles. Since then Charlton Bastian[1] has uttered a similar view, one however that, so far as the dog is concerned, I cannot accept entirely as my own. According to his view those motor centres are centres for the totality of *kinæsthetic impressions.* But we shall soon see that they possess a more broadly measured importance.

They certainly serve, however, also for the apperceptive working up of the kinæsthetic impressions, and it is not without value that we should sum up the totality of these impressions, as Charlton Bastian has done, under the name kinæsthesis. Lately I have, with reference to numerous works of others, tried to show that the totality of these impressions, that are supplied by the various apparatus that serve for orientation and locomotion, are wrought over to conceptions of a lower order touching the relation of the body and of its single parts to space, and that then the organ of consciousness, the cortex, deals with these conceptions of a lower order as with a given whole, without being able to pierce into its details. The place in which this last process, so far as it is possible to fix it, is effected, is according to the results of our researches the gyrus sigmoides, in man therefore a part of the Rolandic region. The determination of this method of viewing the case is of the more importance, because all the corticopetal, and probably, with certain modifications, also all the corticofugal processes proceed in a like manner.

The conceptions of feeling which we obtain from painless handling of the organs of the skin, do not directly belong to the kinæsthetic sensations, although they doubtless stand also in close relations to the motions. I already mentioned above that they also may be in a high degree and in part lastingly injured by lesions of the gyrus sigmoides. It is true that some, as for example Charlton Bastian, have denied that we can learn anything worthy of belief from animals about their conceptions of feeling. But I cannot agree with this view to its full extent. For we do learn sufficiently reliable points as to the internal processes in animals by means of motor reactions that follow with the regularity of law. We may, I concede, still remain in doubt upon the basis of the single experiment, as to whether these reactions take place under the concurrence of conceptions or not. Nevertheless comparative researches give us information about them with a probability that verges upon certainty. I learn then from the dog that has been operated upon, by the unilateral lack of the usual motor reactions, that the sum of his kinæsthetic and tactile impressions is no longer applied to the formation of conceptions for the member affected.

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[1] CHARLTON BASTIAN, "The muscular sense its nature and cortical localisation," BRAIN, April, 1887.

I have not spoken on this occasion of *pain-exciting impressions*, and I shall even now only say briefly that I regard the search for cortical centres for these—a search which has been chiefly practised by English scholars—as hopeless, for the very simple reason that dogs that had been robbed even of their whole cerebrum still showed to Goltz[1] upon the usual attacks the usual utterances of pain. According to this and according to the sum of the further experiments in this line, into which I cannot enter singly, *the feeling* of pain must, analogously to the kinæsthetic sensations, be formed *subcortically*. It is, however, in the highest degree probable that this feeling, in contrast to these sensations, is apperceived in broad sections of the brain cortex as a conception of pain, and that it is only in so far provided with local signs as the pain-exciting stimulus that touches the outer skin is accompanied by the touch stimulus which is accompanied by local signs.

In addition to the motor disturbances mentioned, there comes yet another group, out of which I myself described a number of symptoms as long ago as the year 1874.[2] The most important thing consisted in the fact that the dogs operated upon, as already referred to, with their affected forepaw blindly *step into the air* from the edge of the table, even when their power of sight is not destroyed. They behave then, as I already at that time stated, as far as their fore-paw is concerned, as if for this member the power of sight did not exist, or as if the impressions of sight were not applied to forming conceptions for it. An observation of Goltz as to the tongue points to the same thing, although this scholar has never been willing to join me in my method of viewing the facts. It is, as is well known, not possible to grasp with the fingers a sound dog's tongue that is hanging out; but if we extirpate the corresponding centres it is easy to grasp it. Therefore here also visual conceptions of the dog are no longer applied for the motions of the tongue, which are as for the rest not impaired.

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[1] GOLTZ, "Der Hund ohne Grosshirn," *Pflüger's Archiv.*, Bd. 51, 1892.

[2] HITZIG, "Untersuchungen über das Gehirn," Neue Folge, iv., *Reichert's und Du Bois-Reymond's Archiv.*, 1874, S. 440.

The third group of motor disturbances comprises such as present most or all the characteristics of paralysis as we so well know it in man, and which have been designated by the motion of the paralysis of isolated, intentional motion. I have already mentioned above the description Schiff gave of such a paralysis produced in the case of apes, in so far as such animals run and climb, but are not in a position purposely to grasp a fig with the paralysed hand and to put it into their mouth. Goltz was the first one to describe precisely the same condition for the dog, in so far as dogs, who have learned tricks, lose after the operation the power to give the paw. In the same way we must explain the conduct that I have described in the case of a dog that is hanging in the air, and who is not able to draw away by itself the paw that is hanging down stretched out and paralysed, when it is threatened with a sharp pin.

In all these cases we see that the further conceptions of the animal, the total of which we are accustomed to call his will, in whatever field of the senses they may have arisen, are no longer in a position to excite the motions that are necessary to the carrying out of the will, the moment that the centre I have named is extirpated for the fore-limb.

The relation of the gyrus sigmoides to the faculty of sight assumes a very peculiar position in these considerations. Goltz had originally asserted that the faculty of vision was affected just as much by lesions in the frontal as by lesions in the posterior lobe. Even if he did later, as already mentioned, modify this statement in so far as to declare that the power of sight was more severely and lastingly injured by lesions in the posterior than by lesions in the frontal lobe, that did not change the doctrine that the frontal lobe stood in direct relation to the power of sight. Munk indeed has constantly denied *any* such relation, since he referred the disturbances of vision that occurred in the case of such lesions to subsidiary lesions which were supposed to have affected his sphere of sight. Nothing can be more incorrect than that. I myself had long ago confirmed the simple fact, and the same confirmation has been offered by numerous other scholars, for example, Exner and Paneth and Luciani. Of late, however, I have established the fact that such disturbances of vision arise under circumstances that exclude every subsidiary lesion.

The question now arose whether the dog had only *one* cortical centre of vision in the occipital lobe, or whether he had still another in the motor sphere. This question seemed open to experimental solution on the basis of the following considerations:—If the dog, according to the latter assumption, really possessed two such centres, then the successive lesion of these two centres must produce a summing up of the disturbances of vision. But if we wait until the disturbance of sight that has occurred after a superficial lesion of the occipital lobe has disappeared and then follow it up by a superficial lesion of the gyrus sigmoides, there will not only be no summing up—that is, the vanished disturbance of vision does not reappear in an increased measure—but it will even not appear at all. It follows from this that the disturbance of vision which arises after lesions in the motor zone is only *indirectly* dependent upon this zone, *that the latter does not serve for vision,* and that in consequence the disturbance of vision can only be based upon a process of inhibition that is passed on into the centres of vision.

If anything at all can confirm the doctrine of the localisation of the functions of the brain and remove the last doubts that were conjured up by the Goltz experiments, it is this fact. The true nature of the motor centres appears to be perfectly cleared up by it, and the ways are pointed out by means of which the individual fields of the brain cortex influence each other, as well as the manner of this influence.

If we wished to apply the knowledge thus gained from the *dog* to the *primates*, we should strictly speaking have to draw into consideration to a large extent the comparative physiology of motion. But I must waive that and limit myself to the consideration of the facts lying nearest at hand.

The most striking fact consists in any case in the circumstance that the exceedingly manifold disturbances in the psychical functions of the dog can be induced by an exceedingly slight lesion of the gyrus sigmoides, whereas far larger lesions in the motor zone of the ape give occasion to much less pronounced and complicated phenomena. We observe the same thing, and that in a much more pronounced measure, in the case of lesions which touch the Rolandic region in man. But if we descend in the series of animals, from the dog downwards, we find that the lower the animal stands in this series, the fewer and fewer portions of his motor system are represented in such a way in the brain cortex, that their existence would be provable by means of the electrical stimulus, and that the isolated intentional movement of these portions would be destroyed by the extirpation of the brain cortex. From this we may draw the general law, that on the one hand with the progressive development of the individual and of the brain constantly more and more central organs advance from the subcortical up into the cortical sphere and become subject to the consciousness, and that on the other hand these organs, as the consciousness developes itself more and more, are moved farther apart from each other by the fact that their separate elements differentiate themselves more and more and associate themselves perhaps with new formations which serve consciousness. If the disturbances of sensibility are lacking in the case of relatively large lesions in the Rolandic zone of the ape, and only occur just like temporary disturbances of vision in the case of very great extirpations,—if disturbances of sensibility are wanting in 60% of the cortical lesions of this region in man,—and especially if what Wernicke calls "tactile paralysis" is only met with in comparatively rare cases,—all *this* points by no means to a *fundamental* difference in the organisation and in the physiological functions of the animal and human brain. On the contrary we can only conclude from this that the individual cortex fields must be extirpated to a particular extent and in a particular combination, if those peculiar disturbances are to be produced in the formation of the conceptions which proceed from the physiological changes in the organ of the skin and in the kinæsthetic organs. And further it is necessary so to arrange that extent and combination, as that the formation of these conceptions be not hindered by contemporaneous motor or intellectual paralysis.

I am very far from saying that the relation of sensibility to mobility or the representation of sensibility in the brain cortex of man is fully explained. On the contrary, I think that the most important tasks of the near future lie in this direction. But I also believe that the way in which these tasks are to be solved is designated by the course of thought that I have just sketched.

The other difficulty above mentioned, *The apparent restoration of functions that were apparently lost*, is to be solved by similar considerations.

We have known for a long while that animals of a lower order without a cerebrum or with only a rudimentary cerebrum are capable of very complicated forms of motion that are excited in a reflex way and that are mediated by *special lines of communication* with the intercentral and centrifugal course of which we are but imperfectly acquainted. In higher animals there is associated with this system a second motor system that stands in manifold relations to it and that serves for *conscious arbitrary motion.* This second system starts in the motor centres to which I have referred and takes its course in the pyramid tract, which constantly developes itself more and more with the higher development of the animal. If we extirpate these centres and these tracts it is true that conscious arbitrary motion ceases in the accustomed forms and up to a certain degree in such animals and to a far higher degree in man. Nevertheless I had already said in my first treatise: "it is certain that in this case still further places and courses *must* stand open for some motor impulse or other in order that it may be born and may speed away to the muscles." Since then we have learned, by the experiments of Goltz and Munk, that what I then proved for the centres of the extremities also holds good for experiments with the removal of all motor centres. The experiments of E. A. Schäfer,[1] H. Munk[2] and others, have further taught in what way motor impulses from other than the motor regions of the brain cortex of the animal can become effectual: they have shown that conjugated eye and head motions occur upon excitation of the occipital lobe, that is to say motions that are to be paralleled with the *locomotor* associated motions of the animals. From this alone it was then to be concluded that such associated motions were not started merely by the motor region but also from large districts of the brain cortex.

Another series of experiments leads us to similar conclusions. Schiff[3] had proved that arbitrary motion was not destroyed by cutting through the pyramids. These experiments have with like success been prosecuted of late in a more precise way with manifold variations by Starlinger,[4] Redlich,[5] Prus,[6] H. E. Hering,[7] and others. A series of these experiments showed that the electrical excitation of the cortex, even after the cutting of these courses of communication, still called out epileptic-like and other motor stimulatory effects, and they thus proved that the motor part of the cortex commands those subcortical centres and the courses of communication that radiate from them; these radiating courses probably continue, according to the researches of Redlich and of H. E. Hering, through the tegmentum of the crus cerebri, and according to the researches of Homén,[1] and especially of Redlich, in the spinal marrow, probably in the fasciculus marginalis anterior and in the fasciculus intermedio-lateralis.

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[1] E. A. SCHÄFER, "On Electrical Excitation of the Occipital Lobe," &c. *Proc. Royal Soc.*, 1888, vol. xliii. "Experim. on the Electrical Excitation, &c." BRAIN, 1888.

[2] H. MUNK, "Sehsphäre und Augenbewegungen." Sitzungsberichte, 1890.

[3] SCHIFF, *Lehrbuch der Physiologie*, 1858, 1859, S. 306.

[4] STARLINGER, "Die Durchschneidung beider Pyramiden beim Hunde," *Jahrb. f. Psych.*, Bd. xv., 1897.

[5] REDLICH, "Beiträge zur Anatomie und Physiologie der motorischen Bahnen bei der Katze," *Monatsschr. f. Psych. u. Neurol.*, 1899, Bd. v.

[6] PRUS, "Ueber die Leitungsbahnen und die Pathologie der Rindenepilepsie," *Wien. klin. Wochenschr.*, 1898.

[7] H. E. HERING, "Ueber Grosshirnrindenreizung nach Durchschneidung der Pyramiden oder anderer Teile des centralen Nervensystems mit besonderer Berücksichtigung der Rindenepilepsie," *Wiener klinische Wochenschr.* 1899, No. 33.

That restoration is therefore no longer in the least surprising. If in the cortically maimed dog and in a certain sense also in the ape we at first observe a confused mixing up of, or even a total lack of, the motor expressions, that is to be explained, so far as *obstruction* or shock effects do not occur, by the fact that the remaining motor impulses are given off in an unaccustomed and irregular form; and then with the cessation of the shock effects there gradually arises an accommodation to the new conditions and at the same time a breaking up of the way upon still existing courses of communication. Munk has tried to follow up and explain in a detailed way that which I here call the "breaking up of the way" but I am not able to grant to his essay more than the value of a hypothesis.

If we now, according to the task set us, compare the standpoint of science to-day with the theories that Hughlings Jackson set up thirty years ago, we find, as must be expected from the defects attaching to human research, that some of his views have as a whole or in single parts needed to be corrected, while doubt to-day still reigns as to others, but that the most essential of them have found a brilliant confirmation at the hands of physiological research,—to say nothing of clinical and anatomical research. If we turn our eyes from that which will gradually pass into forgetfulness, we must in the first place emphasise, as an indelible leaf in the history of medicine, Jackson's doctrine of the cortical convulsions, both the general principle of the charging and of the discharge that makes inroads on the neighbouring domains, and the numerous details by which this principle was explained and firmly grounded; in it especially the part determining the muscles in which the cortical fit begins and the sequence in which they are affected by the fits after different beginnings.

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[1] HOMÉN, *Contribution expérimentale à la pathologie et à l'anatomie de la moelle épinière.*

In close connection with this stands the theory which sought the cortical motor centres in the region of the arteria fossæ Sylvii, and especially which brought the centre for the muscles that serve speech into local relations with the Broca convolution.

I am likewise convinced that his view of the cortical combination of motion and sensation has proved to be correct in principle. Both this view and the doctrine of the cortical pressing apart of subcortical unities by new combinations, will certainly in the future play a leading part in our views of mental occurrences, even though it may seem necessary to round out or to correct many a point in detail. The general relation also of the subcortical formations to the cerebral mechanism appears precisely, according to the latest researches, again more in the light in which Hughlings Jackson and the elder school viewed it, although the original argument for those views of Dr. Jackson's proceeded from an erroneous presupposition as to the part played by the internal capsule and the neighbouring gray matter. It may also to-day even still appear doubtful whether these gray masses are capable of an independent primary charging, or only of a secondary one through the cortex.

Taking it all in all we see, even in the part of Dr. Jackson's scientific work that I have described, the work of a man of whom any nation may rightly be proud.

The first physiological treatise in the field which we have entered upon to-day, remained for years unnoticed because of the thunder of the cannon which altered the fate of Central Europe. In the development of more peaceful times a literature that we can scarcely compass has attached itself to this treatise. We, too, we labourers in the realm of the natural sciences, to whatever nation we belong, are soldiers and form an army, but an army that knows of no separation into different camps as a result of national or other interests, an army that is united in the one interest, in the search after truth, in the battle against ignorance and against all the hindrances which some men would like to oppose to our endeavour to reach our ideal aims. It may count as an expression of the mutual character of our cause that I, as a foreigner, was called to-day to do honour to a scholar of this country, and for this reason also I have discharged this flattering task with joy and pride.

THE CONDITION OF THE MEDULLATED FIBRES OF THE CORTEX CEREBRI IN TWENTY-FIVE CASES OF INSANITY.

BY EDWIN GOODALL, M.D.LOND., B.S., M.R.C.P.
Medical Superintendent, Joint Counties Asylum, Carmarthen,
WITH THE ASISSTANCE OF
PEERS MACLULICH, B.A., M.A.DUB.UNIV.
Assistant Medical Officer, Joint Counties Asylum, Carmarthen.

THE subject of the condition of the medullated fibres of the cortex cerebri in persons dying insane has not attracted much attention.

In 1884 Tuczek published his "Contribution to the Pathological Anatomy and Pathology of Dementia Paralytica," the research being concerned, as the title indicates, with a particular form of mental disorder. He found in all cases (seventeen) more or less considerable atrophy of the medullated fibres in certain areas of the cortex. In six control cases of other forms of mental disease, Tuczek got only negative results as regards nerve-fibre atrophy. Zacher, at a later date, examined for disease of the medullated fibres in various kinds of psychoses, and found that these were atrophied in other conditions as well as in paralytic dementia, thus modifying Tuczek's views. Zacher's work is the fullest with which I am acquainted, and I have found a comparison with his results very useful, the investigation being of an analogous nature with the present, though in methods of preparation of specimens and other points there are differences. Tuczek employed Exner's osmic-acid-glycerine method, but the well-known disadvantages attaching to this—such as lack of durability, swelling of sections, cost of osmic acid, the fact that small sections only can be examined, and that in œdematous states of the brain some of the medullated fibres will not stain with osmium—have led to its abandonment in favour of the hæmatoxylin methods based on Weigert's process. A doubt may, however, be permitted as to whether these methods bring out the finest medullated fibres as well as in Exner's process.

Zacher worked with Friedmann's process, but the objection to this and the Friedmann-Flemming modification is, as he recognises, that the outermost zone is liable to be stained too deeply by the osmic acid employed, and thus the fibres there are obscured; further, the preparations are not uncommonly unsuccessful, for some unknown reason.

T. Kaes, whose writings upon the medullated fibres of the cortex are well known, has strongly recommended Wolters's method of staining the fibres. This is also known as the Kultschitzky-Wolters method, because the hæmatoxylin solution used is that recommended by the former (hæmatoxylin pur. cryst. 1·0, alc. abs. q. s. ad solv., acetic acid 2 per cent. sol. 100·0). Sections are left for twenty-four hours in the stain in the incubator. Kaes recommends that they be left for two to three days at 42° to 45°. He considers the method superior to Weigert's, and equal in results to that of Exner. It brings out the finest fibres. Kaes continues to speak well of the method in his later writings, and Passow, writing in 1898 upon the medullated fibres in certain gyri in sane persons, says that after four years' use he cannot speak too highly of the Wolters's method as modified by Kaes. This modification consists in the employment of Flemming's solution in place of Müller's for hardening. By this means Kaes finds that even better results are obtained; the tangential fibres especially are well brought out. Our experience is that an undesirable shrinkage of tissue occurs when Flemming's solution is used; also, that the outermost zone of the cortex is frequently obscured by a black deposit. But as regards the Kultschitzky-Wolters method we are quite able to endorse the experience of Kaes and Passow. We find that the fine fibres are very well brought out and that the durability of the stain is considerable. It is now two years since this work was commenced, and a very large proportion of the sections show undiminished stain. The increased vascularity often present in morbid sections of cortex is well brought out.

In order to secure more certain results we have kept sections, as a matter of routine, in the stain for seven days in the cold, and thereafter for two days at a temperature of 38° to 40°. Brittleness has but seldom been a source of trouble.

Except in the earliest cases, sections were taken from the precentral region, central gyri, temporal and occipital regions. In the earliest cases the section did not comprise more than a single gyrus, or two gyri, with intervening sulcus; but in the later, and majority of cases, large sections were taken, embracing several gyri (up to thirteen), with intervening sulci. It is a possible objection to this plan that the gyri do not receive the individual care in the process of differentiation which would be given were each stained separately. But a certain measure of control in differentiation of the gyri is generally feasible with large sections. Occasionally it happens that a gyrus or two has to be left rather more "chromy" than one would desire, in order that the properly differentiated may be preserved; but this appears often to be due to disease in the gyrus. Everything considered, we are much in favour of the large sections, as giving a very instructive comparative representation of the gyri and their associated sulci. Most of our sections measure 4 to 6·5 cm. by 2 to 4 cm.

For the purpose of this investigation, following Edinger and others, the medullated fibres of the cortex are regarded as composed of the following:—(1) The zonal layer, containing the tangential fibres; (2) the superradiary layer; (3) the interradiary meshwork ("external association-fibres of Meynert."). Between (2) and (3) is placed the condensed layer of transversely-disposed fibres known as Baillarger's layer (or Gennari's, in the occipital region). Lastly, and apart from the above more or less transversely-disposed fibres—which are in this article, for brevity's sake, called "cross-fibres"—the projection-fibres or radii (4) have to be considered.

The origin and connections of the cross-fibres of the cortex—as far as present knowledge permits a statement—may briefly be referred to.

In the zonal area, which corresponds to the molecular or *external* layer of authors, the medullated fibres may be regarded as (*a*) prolongations of the axis-cylinders of the nerve-cells described as existing in that layer by Cajal, namely, the fusiform, triangular, and polygonal nerve-cells; the first two varieties are said to have several axis-cylinders; (*b*) prolongation of the axis-cylinders ascending to the molecular layer from their cells of origin in the pyramidal and polymorphous cell-layers; (*c*) the medullated fibres may also be regarded as partly composed of the terminals of the nerve-fibres, which can be followed into the white matter of the hemisphere, "the cells of origin of which are unknown" (van Gehuchten). The latter may, of course, be situated anywhere in the same or opposite hemisphere.

The superradiary layer and the interradiary meshwork correspond approximately to the layer of pyramidal cells (*middle* layer); the layer of small pyramidal cells answering approximately to the superradiary layer, that of the large pyramidal—including Betz's cells—to the interradiary meshwork.

Lastly, the layer of spindle or polymorphous cells (*internal* layer) is placed in the lowest part of the interradiary meshwork. The medullated fibres of the superradiary layer and the interradiary meshwork may be regarded as composed of (*a*) myelin-enveloped axis-cylinder processes of the cells of the middle and internal layers, which processes are ascending and descending, and of the collaterals of these (if we are justified in regarding these as clothed in myelin in part of their course); (*b*) the nerve-fibres above mentioned under (*c*) will also assist in forming the superradiary layer and interradiary meshwork. The paucity and delicacy of the superradiary fibres, in comparison with the interradiary, may be explained, perhaps, by the smaller size of the cells from which the former spring.

A reference to the order of development of the medullated fibres of the cortex will be opportune here, following the description of Kaes. In the fœtus, between the fifth and sixth months, the cortex is free from medullated fibres. The first to penetrate are the projection-fibres, the fibræ propriæ of Meynert (between cortex and medulla) developing about the same time. Next come the fibres of the interradiary meshwork (Kaes's "external association fibres of Meynert"), and then, about the same time, the fibres of Baillarger's layer and of the zonal layer. Whilst the fibres of these three layers become gradually more numerous, the superradiary layer begins to show (Kaes's "fibre-band of the second and third layer"). The "primary deposit" is now complete. In this is developed the second system of fibres ("der in Gebrauch genonmenen Faser"), thicker and more prominent than the primary, parallel or oblique in disposition. They appear first in the interradiary region, later in the superradiary, then in Baillarger's layer, finally spreading over the whole cortex "as the highest expression of development of the cortical fibres" (Kaes).

Twenty-five brains from cases of mental disorders were examined, embracing cases of mania and melancholia of various degrees, paralytic dementia, delusional insanity, imbecility, and terminal dementia.

In addition, a control specimen was examined from a man aged 46, who died suddenly, and in whom a fibroid state of the heart-muscle was found. The only objection to be brought against this case was the possibility of syphilis as the cause of the cardiac state. But however this may have been, the specimen furnished a large number of gyri which, in the light of other experience, were evidently normal. This control was supplemented by Kaes's description of the cortical medullated fibres in the various regions of the hemisphere in a normal brain. In addition, various of the cases furnished specimens of normal gyri, occurring in association with diseased ones, in the different regions of the hemisphere.

In summarising the condition of the medullated fibres the terms "slightly," "moderately," and "greatly" (or "extremely") degenerate have been used, according as the fibres exhibited the slighter or more aggravated forms of degeneration, tabulated in the scheme according to which the work was done; though, of course, the classes pass into one another. (The condition of "scantiness" is also mentioned separately.)

Thus, with respect to the cross-fibres: if scanty, thin, short, faintly stained, the degeneration is put down as "slight." If, in addition, they are irregularly stained, broken, of uneven calibre, the fibres being mostly small, with large, thick fibres few or absent, the degeneration is "moderate." Whilst it is "great" if the fibres exhibit the above conditions in aggravation together with varicosity and tortuosity. In extreme cases the fibres are represented by rare dots and shreds, or may be absent.

With respect to the projection-fibres or radii: "slight" degeneration connotes the case in which the bundles are thin, with scanty fibres and faint staining, with the terminals of the radii thin, broken, badly stained, irregular in course. "Moderate" degeneration is where, in addition to the above, the bundles fall short, the fibres being broken and thin, unduly wavy in course and irregularly stained. And "great" degeneration connotes the above in aggravation, with uneven calibre of fibres, varicosity and tortuosity of terminals and also of trunks.

The long, thick, deeply-stained fibres met with in the different layers (especially the interradiary and the tangential) in normal specimens—which I take to be the fibres of Kaes's second system—are called, briefly, the "strong" fibres.

The medullated fibres running at right angles to the surface, and passing between the tangential fibres and the deeper parts of the cortex (and probably ascending from or descending to the white matter, in some instances) are called in this article "perpendicular" fibres.

The cases examined are as follows, summarised as much as appears desirable.

(1) H. E.—On admission: acute mania. Causation: influenza and trouble. Clinical course: remained maniacal for four months, then showed partial dementia; phthisis present on admission, progressed, and he improved somewhat in mind. At death: mental state was one of partial

dementia. Cause of death: phthisis. Total duration mental disorder: 6½ months. Age at death: 32.

Frontal gyri.—Tangential and superradiary fibres in fair number, and moderately degenerate. Interradiary meshwork: abundant, but fibres very thin. Radii: normal, excepting terminals, very degenerate. Vascularity + and general, with chrome about the vessels.

Summary.—Moderate degeneration of cross-fibres of outermost two layers; terminals of radii involved in the superradiary degeneration, and especially affected. Vascularity +.

Occipital gyri.—All cross layers appear normal, and radii also. No vascularity; no chrome. Strong and perpendicular fibres in fair number in the various layers.

Summary.—A normal specimen.

In this, the first specimen examined (acute mania passing into mild dementia), gyri were only taken from two regions. Fibre degeneration is moderate in the frontal region, and vascularity proportionately increased.

(2) W. J.—On admission: senile melancholia. Causation: heredity + senile changes. Clinical course: melancholia passing into dementia. At death: complete dementia. Cause of death: senile brain atrophy. Total duration: 4 years. Age at death: 75.

Frontal gyri.—Tangential fibres: exceedingly few and very degenerate. Superradiary: moderately degenerate and very scanty. Interradiary: moderately degenerate and scanty. The cross-fibres are rather worse on the sides. Radii: moderately degenerate, and terminals more so. Vascularity and chrome +, especially on sides.

Summary.—The medullated fibres diseased throughout, most so in the outermost part of cortex (terminals of radii sharing). Tangential about the worst. There are variations in the degree of degeneration in the different parts of the same gyrus (fibres in all layers more affected at one part than another). Maximum increase in vascularity and chrome deposit goes with the maximum fibre-degeneration.

Parietal gyri.—Tangential fibres: very scanty and very degenerate; replaced by connective tissue in parts. Superradiary: rather scanty and moderately degenerated. Strong fibres absent in these two layers. Interradiary: normal, many strong fibres. Radii: trunks normal but terminals very degenerate. Chrome + and general. Vascularity +, but only in foci in outer parts.

Summary.—Cross-fibres degenerate in outer two layers, especially tangential. Terminals of radii share in degeneration. Vascularity is chiefly + with fibre-degeneration.

Occipital gyri.—Tangential fibres: very scanty and very degenerate; connective tissue and chrome deposit in outermost zone. Superradiary still more so. Interradiary: normal. Radii: ditto, terminals very degenerate. Some perpendicular fibres, but degenerate. Vascularity and chrome + and general.

Summary.—Fibres considerably diseased in outermost parts, including terminals of radii. Superradiary worst. Vascular changes not commensurate with those of nerve-fibres.

General summary.—In this case of senile melancholia with dementia the two outermost layers of cross-fibres and the terminals of the radii, which are situated at the level of the superradiary layer, show considerable disease in different parts of the cortex. The conditions are rather worse—the diseased fibres showing deeper in the cortex—in the frontal region. Vascularity and chrome increased, on the whole, in association with fibre-degeneration.

(3) C. W.—On admission: acute melancholia, with ideas of persecution also present. Causation: business troubles. Clinical course: melancholia throughout; attempted suicide. At death: melancholia. Cause of death: pleuro-pneumonia; cardio-arterial degeneration. Total duration: 2½ years. Age at death: 43.

Frontal gyri.—Tangential fibres; very scanty, very degenerate. Superradiary: scanty, very degenerate. Interradiary: extremely scanty, very degenerate. Radii: scanty and degenerate. A few perpendicular fibres, but degenerate. Specimens very vascular and chromy.

Summary.—All cross layers show much degeneration without important distinction, and this extends to radii. Vascularity and chrome + with fibre-changes.

Parietal gyri.—Tangential fibres: ' not scanty, very degenerate. Superradiary: ditto. Interradiary: normal. Radii: ditto. Vascularity and chrome +, but less than in last.

Summary.—Two outermost layers only affected, not scanty, but degenerate. Vascularity and chrome in accordance.

Occipital gyri.—Tangential fibres: very scanty and very degenerate. Superradiary: scanty, very degenerate. Interradiary: very scanty, slightly degenerate. Radii: very scanty and very degenerate. Vascularity and chrome much +.

Summary.—Gyri very degenerate, with vascularity and chrome in association.

Temporal gyri.—Tangential fibres: scanty, moderately degenerate. Superradiary: very scanty, moderately degenerate. Interradiary: scanty, moderately degenerate. Radii: scanty, slightly degenerate. Vascularity +, more than in last; chrome +.

Summary.—Cross-layers moderately degenerate; radii involved in less degree. Vascularity and chrome + in association.

General summary.—In this case of melancholia the medullated fibres generally show disease, the interradiary scarcely better than the two outermost layers, which are equally bad, advanced in the frontal and occipital regions about equally, least in the parietal. The radii sometimes equally involved, but on the whole less. Vascularity and chrome + in association with fibre-degeneration.

(4) J. E.—Admitted three times in three years with acute mania. Discharged recovered twice. On the third occasion remained more or less acutely maniacal for about fifteen months, when she lapsed into a state of chronic mania. This continued until death, weakness of mind becoming more apparent. Cause of death: myocarditis. Total duration: 15 years. Age at death: 65

Parietal gyri, "A."—Tangential fibres: fairly numerous, moderately degenerate. Superradiary: scanty, very degenerate; worse than tangential. Interradiary: numerous, slightly degenerate; good Baillarger layer. Radii: scanty, terminals moderately degenerate. No vascularity; chrome: slight. Perpendicular fibres in fair. number, tortuous. Strong fibres in good number.

Parietal gyri, "B" (another part).—Tangential fibres: scanty, very degenerate. Superradiary: very scanty, very degenerate. Interradiary: ditto. Radii: scanty, very degenerate. Vascularity: slight; chrome: ditto. Perpendicular fibres: scanty, degenerate. Strong fibres less than in "A." A worse specimen than "A."

Summary.—Cross-fibres show considerable degeneration in parietal; these and radii are worse in one part examined than the other. Superradiary fibres are worse than tangential. The Baillarger band and strong and perpendicular fibres are better in the better specimens. Vascularity and chrome not increased at all commensurately with fibre-degeneration.

Occipital gyri, "A."—All cross-layers and radii: moderately degenerate and scanty. Superradiary: as bad as tangential. Terminals of radii: worse than trunks. Vascularity and chrome but slight.

Occipital gyri, "B" (another part).—Tangential fibres: fairly numerous, moderately degenerate. Superradiary: very scanty and very degenerate. Interradiary: fairly numerous, moderately degenerate. Radii: moderately scanty and moderately degenerate. Terminals: worse. Vascularity +, on one side chiefly. Chrome +, chiefly interradiary.

Summary.—Degeneration is chiefly moderate of all cross-layers; superradiary on the whole is worst; interradiary equally affected with tangential. Radii share in the moderate degeneration, and their terminals partake in the worse degeneration of superradiary area. Vascularity and chrome but slightly increased.

Temporal gyri.—Tangential fibres: numerous, good band, but fibres very degenerate. All other cross-fibres and also radii exceedingly scanty and degenerate, and absent in various parts. Strong fibres in tangential band, but none elsewhere. No perpendicular. Vascularity and chrome both somewhat +, but especially so in foci, together.

Summary.—An exceedingly degenerate specimen, with great destruction of fibres, excepting tangential. Vascularity and chrome +, with particular destruction around.

General summary.—In this case of chronic mania with terminal dementia the cross-fibres throughout show considerable degeneration; the radii also. The temporal region is a good deal the worst, followed by the parietal and the occipital. Baillarger, strong, and perpendicular fibres are all better in the better specimens. The superradiary fibres are about the worst, and interradiary are as bad as tangential, even worse than these in the temporal area. The persistence of the tangential band, though composed of very degenerate fibres, in the temporal region, whilst other fibres are largely destroyed, is striking. Vascularity and chrome are +, especially in the worst (temporal) region; elsewhere the increase is not commensurate with fibre-degeneration.

(5) A. J.—On admission: subacute mania. Causation: stated to be shock, in connection with death of mother. Clinical course: subacute mania passing into dementia with periodic outbreaks of excitement and violence. At death: dementia. Cause of death: heart disease. Total duration: 40 years. Age at death: 59.

Frontal gyri.—Tangential fibres: very scanty, slight degeneration. Superradiary: ditto. Interradiary: ditto. Radii: only scanty. Vascularity: considerable; also chrome.

Summary.—All cross-layers but slightly degenerate. Radii probably not degenerate. Vascularity and chrome increased out of proportion to fibre-changes.

Parietal gyri.—Tangential fibres: scanty, slightly degenerate. Superradiary: normal. Interradiary: ditto. Radii: ditto. Vascularity and chrome = 0.

Summary.—Normal, except slight tangential changes.

Occipital gyri.—Tangential fibres: very scanty and moderately degenerate. Superradiary: ditto. Interradiary: scanty and very degenerate, the Gennari band thin over the summit. Radii: very degenerate, including terminals (even worse). Vascularity +, capillary, and chiefly interradiary. Chrome: normal. Some perpendicular fibres, but very scanty and very degenerate.

Summary.—All cross-layers degenerate, but deepest layer most so, and radii even worse. Vascularity = + in worst fibre area. Chrome = 0.

Temporal gyri.—Tangential fibres: moderately degenerate. Superradiary: extremely scanty, very degenerate. Interradiary: ditto. Radii: only scanty. Vascularity and chrome + and marked.

Summary.—All cross-layers degenerate, the outermost least so. Radii escape.

General summary.—In this case of subacute mania with terminal dementia the cross-fibres show degeneration in all regions, though the parietal is almost normal; the temporal region perhaps the worst, though occipital is scarcely better; frontal but slightly affected. The interradiary layer is the worst in the occipital, the superradiary and interradiary in the temporal, the tangential being less affected. The radii are only scanty in the otherwise very degenerate temporal, very degenerate in the occipital. The normal area is neither vascular nor chromy, whilst the others show vascularity and chrome +.

(6) R. D.—On admission: acute mania. Causation: unknown. Clinical course: the condition became gradually chronic: dementia came on eight years after admission; remained a noisy chronic maniac, with weakness of mind, till death from pelvic abscess. Total duration: 33 years. Age at death: 54.

Frontal gyri.—Tangential fibres: numerous, moderately degenerate. Superradiary: numerous, very degenerate. Interradiary: numerous, moderately degenerate. Radii: normal. Vascularity and chrome = 0.

Summary.—All cross-layers show degeneration, especially superradiary. No scantiness of fibres. Otherwise normal.

Parietal gyri.—Tangential fibres: numerous, moderately degenerate. Superradiary: extremely scanty, moderately degenerate. Interradiary: fairly numerous, slightly degenerate. Radii: normal; terminals degenerate. Vascularity and chrome = 0.

Summary.—All cross-layers show degeneration, especially superradiary; terminals of radii involved with them.

Occipital gyri.—Tangential fibres: extremely scanty (almost absent), very degenerate. Superradiary: fairly numerous, moderately degenerate; some strong fibres. Interradiary: not scanty, but very degenerate. Radii: not scanty, moderately degenerate. Vascularity and chrome +, latter chiefly about vessels.

Summary.—All cross-fibres degenerate, the outermost most so. Radii moderately involved. Vascularity and chrome + with fibre-degeneration.

Temporal gyri.—Tangential fibres: normal. Superradiary: very scanty (hardly exist), very degenerate. Interradiary: extremely scanty, moderately degenerate. Radii: fibres scanty only. Vascularity + and chrome much +.

Summary.—Tangential fibres: normal. Superradiary: much the worst of remaining layers. Vascularity and chrome + in conjunction with fibre-degeneration.

General summary.—In this case of chronic mania with terminal dementia the cross-fibres are considerably diseased throughout, principally the outermost two layers, in varying measure, with the exception of the tangential fibres in the temporal area, which are normal. The occipital region is worst; then follow in order: parietal, temporal, frontal. In the three last regions the superradiary layer is the worst. The radii are only moderately involved even in the worst specimens. Vascularity and chrome not always associated with fibre-degeneration, but they are increased in the worst specimens.

(7) L. P.—On admission: mania, with delusions of persecution. Causation: unknown (heredity present). Clinical course: delusions marked throughout; very hostile, raving frequently. At death: delusional insanity with dementia. Cause of death: phthisis. Total duration: 7¾ years. Age at death: 62.

Frontal gyri.—Tangential fibres: very scanty and very degenerate. Superradiary: scanty and very degenerate. Interradiary: scanty, moderate degeneration. Radii: very scanty, slightly degenerate. Vascularity + and chrome in patches.

Summary.—Degeneration of all cross-layers, especially of two outermost. Radii: involved in lesser degree, and vascularity and chrome +.

Parietal gyri.—Tangential fibres: scanty, very degenerate. Superradiary: very scanty, very degenerate. Interradiary: normal. Radii: scanty, slightly degenerate. Vascularity and chrome = 0.

Summary.—Degeneration of two outermost layers, and radii involved in minor degree. No commensurate increase of vascularity and chrome.

Occipital gyri.—Tangential fibres: very scanty, moderately degenerate. Superradiary: very scanty, moderately degenerate. Interradiary: scanty, slightly degenerate. Radii: scanty, moderately degenerate. Vascularity and chrome rather +.

Summary.—Cross-fibres: moderately degenerate, especially outer two layers. Radii: almost equally involved. Vascularity and chrome increased about proportionately.

Temporal gyri.—Tangential fibres: very scanty, moderately degenerate. Superradiary: very scanty (almost absent), very degenerate. Interradiary: scanty, moderately degenerate. Radii: scanty, very degenerate. Vascularity: much +, and chrome +.

Summary.—Cross-layers and radii all degenerate, the superradiary the worst. Vascularity and chrome proportionately increased.

General summary.—In this case of delusional insanity, with terminal dementia, the cross-fibres are degenerate, in considerable degree, in the different cerebral regions, the outermost two layers being chiefly affected. The superradiary is as much involved as the tangential. The radii are involved in a lesser degree, except in the temporal region (the worst), where they are equally affected with the worst of the cross-fibres. Vascularity and chrome are associated with the fibre-degeneration. The temporal region is the worst, followed by the frontal, occipital, and parietal in order.

(8) J. M.—On admission: acute mania. Causation: heredity, otherwise unknown. Clinical course: acute mania with occasional stupor. At death: mania. Cause of death: exhaustion from mania. Total duration: 1½ years. Age at death: 32.

Frontal gyri.—Tangential fibres: very scanty and very degenerate. Superradiary: ditto. Interradiary: ditto. Radii: numerous, moderately degenerated. Vascularity and chrome = 0.

Summary.—All cross-layers: very degenerate. Radii: moderately involved. No proportionate increase in vascularity and chrome.

Parietal gyri.—Tangential fibres: fairly numerous, very degenerate. Superradiary: ditto. Interradiary: normal. Radii: ditto. Vascularity and chrome = 0.

Summary.—The two outermost layers degenerate, otherwise normal.

Occipital gyri.—Tangential fibres: scanty, moderately degenerate. Superradiary: ditto. Interradiary: ditto. Radii: scanty, very slightly degenerate. Terminals: degenerate. Vascularity and chrome = 0.

Summary.—All cross-layers degenerate in moderate degree. Radii: only slightly affected, but their terminals more so. Vascularity and chrome not involved with fibre-changes.

Temporal gyri.—Tangential fibres: not scanty, moderately degenerate. Superradiary: almost absent, very degenerate. Interradiary: scanty and very degenerate. Radii: ditto. Vascularity and chrome = 0.

Summary.—All cross-layers degenerate, most so in deeper parts. Superradiary: worst. Radii: equally involved. Vascularity and chrome do not follow fibre-degeneration.

General summary.—In this case of acute mania the cross-fibres are not normal in any region, and are mostly notably degenerate. The frontal region is about the worst, closely followed by the temporal; then come the parietal and occipital, about equally involved. The superradiary layer is as much affected as the tangential, and sometimes more so. The radii are less affected than the cross-fibres on the whole, though equally involved in the temporal region. There is a striking absence of vascularity and chrome.

(9) E. W.—On admission: delusional insanity (ideas of persecution). Causation unknown. Clinical course: remained same throughout, very hostile. At death: the same. Cause of death: aortic valvular disease. Total duration insanity: 6 years. Age at death: 37.

Frontal gyri.—Tangential fibres: extremely scanty and very degenerate. Superradiary: ditto. Interradiary: ditto. Radii: scanty and very degenerate. Vascularity +. Chrome = 0.

Summary.—All cross-layers and radii very degenerate. Vascularity is increased therewith.

Parietal gyri.—Tangential fibres: extremely scanty and very degenerate. Superradiary: ditto. Interradiary: ditto. Radii: scanty, very degenerate. Vascularity and chrome = 0.

Summary.—All cross-layers and radii very degenerate. No corresponding increase of vascularity and chrome.

Occipital gyri.—Tangential fibres: extremely scanty and very degenerate. Superradiary: ditto. Interradiary: ditto. Radii: ditto. Vascularity and chrome = 0.

Summary.—As in last.

General Summary.—In this case of delusional insanity the cross-fibres are extremely degenerate and the radii equally so. All parts equally bad. Vascularity and chrome are not increased in two of the regions, and their increase may be said to be not at all commensurate with fibre-degeneration.

(10) E. G.—On admission: acute melancholia. Discharged and remained out five to six years; readmitted in same state with some mental weakness also. Causation:

unknown. Clinical course: melancholia, passing into dementia. At death: dementia. Cause of death: chronic renal disease. Total duration: 14 to 15 years. Age at death: 72.

Parietal gyri.—Tangential fibres: very scanty, moderately degenerate. Superradiary: very scanty, moderately degenerate. Interradiary: normal. Radii: ditto. Vascularity and chrome = 0.

Summary.—The outermost two layers show moderate degeneration; otherwise normal.

Occipital gyri—Tangential fibres: very scanty and very degenerate. Superradiary: ditto. Interradiary: ditto. Radii: ditto. Vascularity and chrome = 0.

Summary.—All cross-layers and radii very degenerate, and equally so. Vascularity and chrome, on the contrary, not affected.

Temporal gyri.—Tangential fibres: not scanty, slightly degenerate. Superradiary: scanty, moderately degenerate, worse than former layer. Interradiary: ditto. Baillarger band exists. Radii: scanty and degenerate. Vascularity = 0. Chrome = rather + in superradiary and interradiary layers.

Summary.—The cross-fibres degenerate in varying degree, the tangential rather less than deeper ones. Radii involved equally with latter. No disease in vascularity but there is in chrome.

General Summary.—In this case of chronic melancholia, passing into dementia, the cross-fibres show varying degrees of degeneration (superradiary the worst), being worst in the occipital region, followed successively by the temporal and parietal regions. The radii pretty well follow suit, worst in occipital and normal in parietal. Vascularity and chrome do not follow fibre-degeneration, there being no vascularity at all and only very localised chrome.

(11) J. T.—On admission: subacute mania. Causation: no certain cause. Clinical course: subacute mania, passing into dementia shortly before death. Cause of death: broncho-pneumonia. Total duration: 6 months. Age at death: 58.

Frontal gyri.—Tangential fibres: rather scanty and very degenerate. Superradiary: fairly numerous, very degenerate. Interradiary: numerous, moderately degenerate. Radii: scanty, moderately degenerate; terminals more so. Vascularity and chrome = 0.

Summary.—Cross-fibres degenerate, especially the two outermost layers. Radii less degenerate than these but terminals equally bad. Vascularity and chrome not increased with fibre-changes.

Parietal gyri.—Tangential fibres: numerous but extremely degenerate. Superradiary: numerous, but less degenerate. Interradiary: numerous but less degenerate still. Radii: numerous; moderately degenerate. Vascularity = 0. Chrome only in interradiary.

Summary.—All cross-layers and radii show degeneration, worst and marked in outermost layer and progressively less from without. Vascularity and chrome not increased with fibre-degeneration.

Temporal gyri.—Tangential fibres: very scanty and very degenerate. Superradiary: ditto. Interradiary: numerous, moderately degenerate. Radii: scanty, moderately degenerate. Terminals very degenerate. Vascularity and chrome = 0.

Summary.—Cross-fibres degenerate, especially of outermost two layers. Radii less affected than these, but terminals equally bad. Vascularity and chrome not increased with fibre-changes.

General summary.—In this case of subacute mania, passing into dementia, the cross-fibres show considerable degeneration in all regions, the temporal being rather the worst, the other two regions about equally affected. In all parts the two outermost layers are most involved, the tangential being the worst in one. The radii are less affected but their terminals share in the degeneration of the layer in which they lie. Vascularity and chrome are singularly absent, notwithstanding fibre-degeneration.

(12) M. J.—On admission: subacute mania. Causation: unknown. Clinical course: recurrent mania; ultimately

some dementia. At death: in same mental state. Cause of death: general tuberculosis. Total duration: 31 years. Age at death: 52.

Frontal gyri.—Tangential fibres: scanty and very degenerate. Superradiary: extremely scanty and very degenerate (worse). Interradiary: ditto. Radii: very scanty and very degenerate. Vascularity = +, slightly.

Summary.—All cross-layers and radii very degenerate. Superradiary and probably interradiary worse than tangential. Vascularity is not commensurate with fibre-changes.

Parietal gyri.—Tangential fibres: fairly numerous and moderately degenerate. Superradiary: extremely scanty and very degenerate. Interradiary: numerous, but moderately degenerate. Radii: very degenerate, involved in chrome. Vascularity = 0, but chrome much +, especially interradiary.

Summary.—All cross-layers degenerate, superradiary the worst. Radii equally involved with the worst. Vascularity does not go with fibre-degeneration, but chrome is much +.

Occipital gyri.—Tangential fibres: fairly numerous, moderately degenerate. Superradiary: scanty and very degenerate. Interradiary: scanty, moderately degenerate. Radii: scanty, very degenerate. Vascularity = 0; chrome = +.

Summary.—All cross-layers show degeneration, superradiary the worst, next the interradiary, and radii equally degenerate with worst. Vascularity does not go with fibre-changes, but chrome does.

Temporal gyri.—Tangential fibres: fairly numerous, very degenerate. Superradiary: very scanty and very degenerate (worse). Interradiary: numerous, moderately degenerate. Radii: scanty, very degenerate. Vascularity = 0; chrome +, chiefly interradiary.

Summary.—All cross-layers degenerate, superradiary worst. Radii equally degenerate. Vascularity does not go with fibre-changes, but chrome does.

General summary.—In this case of recurrent mania with terminal dementia the cross-fibres and radii show considerable degeneration in the different parts of the hemisphere, the frontal area being the worst. It is noteworthy that in all regions the superradiary layer is worse than the tangential or interradiary, and the latter is nearly as much affected as the tangential. Further, the radii are equally degenerate with the cross-fibres. With much fibre-degeneration there is little or no vascular increase, whilst chrome is increased.

(13) H. D.—On admission: chronic melancholia with some dementia. Causation: not clear; came on gradually. Clinical course: the same condition until death, which resulted from cardiac mural disease. Total duration: 3½ years. Age at death: 57.

Frontal gyri.—Tangential fibres: not scanty, moderately degenerate. Superradiary: scanty, very degenerate. Interradiary: ditto. Radii: scanty, moderately degenerate; terminals very much so. Vascularity = 0; chrome + slightly.

Summary.—All cross-layers show degeneration; superradiary and interradiary most, and equally; radii trunks moderately, terminals greatly, affected. Vascularity not increased with fibre changes.

Parietal gyri.—Tangential fibres: not scanty, moderately degenerate. Superradiary: scanty, very degenerate. Interradiary: fairly numerous, moderately degenerate. Radii: scanty, very degenerate. Vascularity = 0; chrome +, slightly.

Summary.—All cross-layers show degeneration, superradiary most, interradiary as much as tangential. Radii as affected as superradiary. Vascularity not increased with fibre changes.

Temporal gyri.—Tangential fibres: not scanty, very degenerate. Superradiary: scanty, moderately degenerate. Interradiary: numerous, moderately degenerate. Radii: very scanty and very degenerate. Vascularity = 0; chrome +, slightly.

Summary.—All cross-layers show degeneration, tangential the most. Radii are even worse than cross-layers. Vascularity not increased with fibre-changes.

General summary.—In this case of chronic melancholia with some dementia the cross-fibres and radii show considerable degeneration in the different regions examined, which are about equally affected. The superradiary affected to a rather greater degree than the other cross-fibres, interradiary as much diseased as tangential. The radii are diseased in an extraordinary degree, equally with the worst cross-fibres. With much fibre-degeneration no increase in vascularity, and chrome also shows slight increase.

(14) L. B.—On admission: acute mania. Causation: the puerperal state. Clinical course: acute mania throughout. At death: the same. Cause of death: exhaustion and acute enteritis. Total duration: 5½ months. Age at death: 26.

Frontal gyri.—Tangential fibres: numerous, moderately degenerate. Superradiary: ditto. Interradiary: normal. Radii: ditto. Vascularity = 0; chrome +, general.

Summary.—Normal, with exception of moderate degeneration of two outermost layers.

Parietal gyri.—Tangential fibres: normal. Superradiary: slightly degenerate. Interradiary: normal. Radii: ditto. Normal perpendiculars. Vascularity and chrome = 0.

Summary.—Normal, except from slight superradiary degeneration.

Occipital gyri.—Tangential fibres: numerous, very degenerate. Superradiary: ditto. Interradiary: ditto. Radii: extremely degenerate and scanty. Vascularity = 0; chrome +, general, deep.

Summary.—All cross-layers show much degeneration, though fibres are numerous. Radii are rather worse. No increase in vascularity, but chrome is +.

Temporal gyri.—Tangential fibres: normal. Superradiary: ditto. Interradiary: ditto. Radii: scanty, moderately degenerate; terminals normal. Vascularity and chrome = 0.

Summary.—Cross-layers normal. Radii moderately degenerate. Vascularity and chrome not present.

General summary.—In this case of acute puerperal mania the occipital region shows the most degeneration by far, the frontal comes next. The parietal and temporal are not far from normal, the latter showing degenerate radii and normal cross-layers—a very unusual condition. On the whole the outermost two layers are most affected, superradiary as much as tangential. Vascularity is not present in conjunction with fibre-degeneration, whereas chrome is, in the most degenerate parts.

(15) L. B.—On admission: acute melancholia. Causation: the puerperal state. Clinical course: acute melancholia throughout. At death: the same. Cause of death: exhaustion. Age at death: 23. Total duration, 2½ years.

Frontal gyri.—Tangential fibres: extremely scanty and very degenerate. Superradiary: ditto. Interradiary: ditto. Radii: scanty and very degenerate. Vascularity and chrome +.

Summary.—All cross-layers and radii very degenerate, with vascularity and chrome increased proportionately.

Parietal gyri.—Tangential fibres: scanty and degenerate. Superradiary: ditto. Interradiary: normal. Radii: ditto. Vascularity +, slight; chrome = 0.

Summary.—The two outermost cross-layers degenerate, but less than last. Vascularity in accordance with fibre-changes.

Temporal gyri.—Tangential fibres: very scanty and moderately degenerate. Superradiary: scanty and degenerate. Interradiary: ditto. Radii: scanty and very degenerate. Vascularity +, slight; chrome = 0.

Summary.—All cross layers show degeneration, chiefly outermost, but more marked. Radii: rather worse. Vascularity only slight.

Occipital gyri.—Tangential fibres: very scanty and very degenerate. Superradiary: numerous, very degenerate. Interradiary: numerous, degenerate. Radii: numerous, slightly degenerate. Terminals extremely so. Vascularity and chrome only locally + (superradiary).

Summary.—All cross-layers show degeneration, especially outermost. Terminals of radii involved with superradiary. Vascularity and chrome scarcely proportionately increased.

General summary. — In this case of acute puerperal melancholia the cross-fibres show considerable degeneration in the various parts of the hemisphere examined (especially the outermost two layers), the frontal region being the worst, the parietal showing least, the other two regions about equally affected. The radii show considerable degeneration in the worst area, but escape in the part with least degeneration. Vascularity and chrome are increased in the worst area, but do not go *pari passu* with fibre changes in the other parts.

(16) A. J.—On admission: paralytic dementia, demented type. Causation: heredity +, ? alcoholism. Clinical course: demented type of general paralysis throughout, resistive, helpless. At death: ditto. Cause of death: paralytic dementia. Age at death: 53. Total duration: about 10 months.

Frontal gyri (6).—Tangential fibres: scanty and very degenerate, with some variation in degree in different gyri. Superradiary: very scanty and very degenerate in all; worse than last. Interradiary: ditto. Radii: good in some gyri, but very degenerate on the whole. Vascularity = + in majority gyri; two are not vascular. Chrome = + in all.

Summary.—All cross-layers show much degeneration with some variation in degree in different gyri. Superradiary and interradiary the worst, and equally. Radii: usually very degenerate. Vascularity and chrome: generally + with fibre-degeneration.

Sulci (5).—Connected with the gyri. The cross-fibres are in general numerous, and show moderate degeneration, especially outermost layer. Variations between different sulci. Vascularity and chrome + in all save one.

Parietal gyri (5).—Tangential fibres: variations exist in different gyri and also in different parts of individual gyri. Generally degenerate; most over summit. Superradiary: ditto. Interradiary: not scanty but degenerate. Radii: generally degenerate; the same variations. Baillarger well-marked in most gyri. Terminals worse. Vascularity +, capillary uniform. Chrome only slightly +. Perpendicular fibres exist; very degenerate. One gyrus normal.

Summary.—General degeneration of cross-layers and radii, with variations in degree in different gyri and in different parts of individual gyri. Summit of gyrus generally the worst site. Vascularity +, but chrome less so. Persistence of Baillarger. A normal gyrus present with degenerate.

Sulci (4).—The fibres of the two outermost layers scanty and degenerate, those of interradiary vary, some being normal. Vascularity +, capillary.

Occipital gyri (4).—Tangential fibres: in general very scanty and very degenerate. Variations similar to last. Superradiary: in all very scanty and degenerate. Interradiary: in general very scanty and degenerate. Radii: scanty and degenerate in two, normal in two. Terminals only escape in one. Vascularity +, chiefly superradiary. Chrome + in some, not in all.

Summary.—General degeneration of cross-layers, with variations between gyri. Radii less generally affected. Vascularity + with fibre-changes. Chrome is more variable.

Sulci (5).—Fibres hardly exist, and are very degenerate in majority. Normal in remainder. Vascularity = + in some, none in others, without reference to fibre degeneration.

General summary.—In this case of paralytic dementia the cross-layers and the radii are much degenerated in the different parts of the hemisphere. The cross-layers about equally involved. Radii scarcely better. Variations between neighbouring gyri and in individual gyri in different parts. The different parts about equally affected, though frontal more uniformly than others. Vascularity = + with fibre-changes. Chrome is also −, but more variable in this respect. As regards sulci there is much variation; the majority show degeneration, but not so much as in gyri. Some are normal. Most show vascularity and chrome +.

(17) J. H.—On admission: paralytic dementia, maniacal type. Causation: not clear; had been seafaring man, and alcohol very probable. Clinical course: maniacal type; general paralysis throughout. At death: demented; died in convulsions. Cause of death: general paralysis of the insane. Age at death: 54. Total duration: 2 years.

Frontal "A."—Tangential fibres: very scanty, very degenerate. Superradiary: ditto. Interradiary: ditto. Radii: ditto. Vascularity and chrome + (extreme).

Summary.—All fibres, cross and radii, very degenerate. Vascularity and chrome associated therewith.

Frontal "B" (another part).—Tangential fibres: extremely scanty and extremely degenerate. Superradiary: ditto. Interradiary: ditto. Radii: very scanty and very degenerate. Vascularity and chrome + (extreme).

Summary.—Rather worse than "A."

Frontal "C" (another part).—Tangential fibres: extremely scanty and extremely degenerate. Superradiary: ditto. Interradiary: ditto. Radii: ditto. Vascularity and chrome + (extreme).

Summary.—As in "B."

Frontal "D" (another part) *gyri* (5).—Tangential fibres: absent. Superradiary: ditto. Interradiary: ditto. Radii: scanty and degenerate. Vascularity and chrome + (extreme). Chrome around the vessels especially.

Summary.—A worse specimen than others. Cross-fibres: absent. Radii: less affected. Vascularity and chrome go with fibre-changes.

Summary for frontal area.—Very marked degeneration of cross-layers and radii, with some variations in different parts of the lobe. The cross-fibres absent in some parts. Vascularity and chrome greatly +, with fibre-degeneration.

Sulci (5).—Except very scanty and very degenerate intermediary, no cross-fibres. Vascularity and chrome + in all.

Parietal gyri (4).—Tangential fibres: very scanty and very degenerate. Variations in different gyri and in individual gyri. Superradiary: ditto. Interradiary: very scanty, slight degeneration; variations as above. Baillarger: well marked. Radii: normal in two, scanty and degenerate in other two. Vascularity and chrome greatly + (latter around vessels).

Summary.—All cross-layers show degeneration, marked in outer two. Variations between gyri and parts of a gyrus. Radii: less affected. Vascularity and chrome + with fibre-degeneration.

Sulci (3 and 4).—Fibres degenerate. Vascularity and chrome +.

Occipital gyri (4).—Tangential fibres almost absent, very degenerate. Superradiary: ditto. Interradiarry: much the same, but variations between gyri. Radii: extremely scanty and very degenerate. Variations as above.. Vascularity and chrome +, latter around vessels.

Summary.—All cross-layers show great degeneration, interradiary less consistently than others; latter remark also applies to radii. Vascularity and chrome + with fibre changes.

Sulci (5).—Fibres extremely degenerate and vascularity and chrome +, slightly.

Temporal gyri (5).—Tangential fibres: absent. Superradiary: ditto. Interradiary scanty and extremely degenerate. Radii: ditto. Vascularity and chrome greatly +, latter about vessels.

Summary.—Extreme degeneration of all medullated fibres. Vascularity and chrome + in proportion.

Sulci (3 and 4).—Vascularity and chrome greatly +. Fibres absent, except very few and degenerate interradiary.

General summary.—In this case of paralytic dementia the medullated fibres, especially the cross-fibres, show very marked degeneration (to the extent of complete destruction sometimes) in all regions of the hemisphere, without appreciable distinction, except for the parietal, which is rather less affected. At the site of greatest disease, in a given area, the gravity of the disease does not allow of any variations between gyri and parts of these; elsewhere these variations are seen. The degeneration is so great that Baillarger's band is no longer to be made out, except rarely, where the conditions are not so extreme (parietal). On the whole, the two outermost layers are the worst parts of the cortex, and are equally involved. Vascular disease, extreme and general, with fibre-degeneration. Chrome greatly + around vessels.

In the *sulci* the fibre-degeneration and vascularity and chrome are about equal to the gyri.

(18) G. E. On admission: imbecile (noisy, violent, impulsive). Causation: heredity, intensified by alcoholic

habits. Clinical course: the same throughout. At death: the same. Cause of death: Landry's paralysis (ten days' duration). Age at death: 30.

Frontal gyri (3).—Tangential fibres: scanty, extremely degenerate. No notable variations between different gyri; local variations in individual cases. Superradiary: very scanty, extremely degenerate. Some variations. Interradiary: ditto. Baillarger present. Radii: very scanty and extremely degenerate; worst over summit. Vascularity +, also chrome, but not always together, and not general.

Summary.—All cross-layers and radii show extreme degeneration with local variations in degree within the gyrus. Baillarger band escapes the other interradiary degeneration. Vascularity and chrome +, but not general.

Sulci.—Fibres degenerate and scanty. Interradiary: better than others. Vascularity and chrome +.

Central "A" gyri (3).—Tangential fibres: slightly scanty, moderately degenerate; worse at summit. Superradiary: very scanty and very degenerate. Interradiary: slightly scanty, very degenerate. Variations between gyri. Radii: scanty and degenerate; worse over summit. Vascularity and chrome: slight.

Summary.—All cross-layers and radii show degeneration, the superradiary about the worst. Conditions rather worse at summit. The interradiary vary in degeneration in different gyri. Vascularity and chrome: slight, and not in proportion to above changes.

Central "B" (another part) *gyri* (3).—Tangential fibres: scanty and moderately degenerate. Variations noted in individual gyri. Superradiary: scanty and very degenerate. Interradiary: scanty and degenerate. Radii: scanty and degenerate; terminals worse. Vascularity +, chiefly interradiary, and chrome + about vessels.

Summary.—All cross-layers and radii scanty and degenerate, with superradiary about the worst. Variations as respects tangential: as above. Vascularity and chrome +, localised.

Summary, central.—All cross-layers and radii show degeneration, superradiary rather the worst. Some variations between gyri and in gyri, but minor. Vascularity and chrome not striking; scarcely proportionate to other changes.

Sulci (3).—Fibre-degeneration, two outermost layers especially. Vascularity +. Chrome = 0.

Occipital "A" gyri (7).—Tangential fibres: very scanty and very degenerate. Gyri equally bad. Variations between gyri and between parts of individual gyri, generally worst over summit. Superradiary: very scanty and very degenerate. Gyri: unequally affected. Interradiary: scanty, moderately affected. Variations as above. One gyrus normal. Radii: scanty and degenerate, especially terminals. Two gyri normal. Vascularity + greatly, and worst with fibre-changes. Chrome is more irregular. Strong fibres absent.

Summary.—The cross-layers are very degenerate, especially the outer two. Variations in degree as above. Radii: mostly degenerate, and terminals worse. Vascularity + with above changes.

Occipital "B."—A similar summary to "A." Vascularity is +, but with variations in different gyri.

Sulci (7).—Fibres normal. Vascularity +; chrome much less so.

Temporal gyri (5).—Tangential fibres: much variation, some normal, some very scanty and degenerate in parts of a gyrus. Superradiary: ditto. Interradiary: normal. Radii: ditto. Vascularity = +, chiefly outermost layers. Chrome +, in deeper layers.

Summary.—A better specimen than the preceding; some gyri normal; in others the two outermost layers show degeneration with variations between gyri and in individual gyri. Vascularity + in affected parts; chrome +, but does not follow vascularity.

Sulcus (1).—Fibres normal; vascularity only slight.

General summary.—In this case of imbecility with excess in alcohol the medullated fibres show considerable degeneration, the frontal and central regions worse than the occipital and temporal: the first-named most, the last least. There are variations between gyri and parts of individual gyri in the different regions. Vascularity is generally + in conjunction with fibre-degeneration, but not a striking feature. Chrome is not marked and not regularly associated with the vascular change. As regards *sulci*, the fibres are the worst in those connected with the worst gyri—frontal and central; and vascularity and chrome most marked in the same.

(19) J. W. On admission: paralytic dementia, maniacal type. Causation: overstrain. Clinical course: maniacal type, general paralysis until death. Total duration: 5½ months. Age at death: 37.

Frontal "A" *gyri* (5).—Tangential fibres: extremely scant, extremely degenerate all through. Superradiary: ditto, but rather less scanty. Interradiary: ditto, one gyrus rather less scanty. Radii: scanty, moderately degenerate, terminals very degenerate, one gyrus worst. Vascularity greatly +, chiefly super- and interradiary. Chrome: ditto, obscures all in places. Pia greatly thickened and infiltrated with round cells. Strong fibres practically absent.

Summary. — Extreme degeneration of cross-layers throughout, tangential rather the worst. Radii less affected, excepting terminals much so. Vascularity and chrome go with fibre-changes.

Frontal "A¹" (same part, 5 gyri). All as above. One gyrus shows normal radii.

Frontal "B" (another part, 1 gyrus).—Fibres and radii practically as in last two. Superradiary worse than tangential. Vascularity +, chiefly outermost two layers. Chrome: slight, diffuse.

Summary.—Same degenerations as "A"; superradiary worst. Vascularity has rather different seat of election; chrome is less than in "A."

Frontal "C" (another part, 2 gyri).—Tangential fibres as in previous in one gyrus, better in the other. Superradiary: as in previous. Interradiary: ditto. Radii: normal. Vascularity and chrome +.

Summary.—All cross-layers degenerate; tangential shows variations. Radii: normal. Vascularity and chrome go with fibre-changes.

Frontal "D" (another part, 2 gyri).—Cross-layers and radii: as in "A," and even worse conditions obtain. Two outermost the worst.

Summary, frontal region.—Degeneration of cross-fibres is great throughout, variations unimportant. The two outermost layers are the worst, but superradiary are as affected, at least, as tangential. Radii not so regularly or extensively affected as the cross-layers. Vascularity and chrome commonly much +, with varying seats of greatest intensity. Strong and perpendicular fibres are practically absent.

In seven *sulci* examined the fibres are very scanty and degenerate, the absence of the sweep of external association fibres of Meynert in some sulci is striking. Vascularity and chrome +.

Frontal near ascending frontal "A" (5 gyri).—Tangential fibres: very scanty and very degenerate in all, with variations in degree, in difference, and in individual gyri. Superradial: very scanty and very degenerate. Interradiary: fairly numerous, moderately degenerate. Radii: majority normal as regards trunks, but terminals are degenerate; minority very scanty and degenerate. Vascularity and chrome + in all.

Summary.—Cross-layers degenerate in all, the two outermost chiefly, with variations, as above. Radii less affected, but variations, and terminals always involved. Vascularity and chrome go with the fibre-changes.

Sulci (2).—Tangential fibres: scanty and degenerate. Vascularity and chrome +

Frontal near ascending frontal "B" (another part, 5 gyri).—Tangential fibres: very scanty and very degenerate in all, with variations between gyri. Superradiary: ditto. Interradiary: not scanty but degenerate, but worse in these respects in a minority. Extreme tortuosity in one gyrus. Baillarger well marked in some. Radii: numerous in three, scanty in two; varying degrees of degeneration. Normal in one gyrus. Vascularity greatly +, with variations in different parts individual gyri. Chrome: ditto.

Summary.—All cross-fibres show great degeneration, especially outermost two, with variations, as described. Radii show less. Vascularity and chrome follow fibre-changes.

Sulci (3 and 4).—Fibres degenerate, involving interradiary in worst cases. Vascularity + in all, but chrome only in some.

Summary of frontal near ascending frontal.—Great degeneration of all cross-layers, especially of outermost two layers, with variations in degree between different gyri and locally in individual gyri. Radii: generally but not universally affected, and less than previous. Terminals worst. Strong and perpendicular fibres are scanty and degenerate. Vascularity and chrome +, with fibre-degeneration.

Sulci.—The fibres degenerate in general, but less notably.

Central "A" (5 gyri).—Tangential fibres: fairly numerous, all degenerate in different degrees in different gyri. Much worse in No. 5. Superradiary: scanty and degenerate, with similar variations, worst in No. 5; Nos. 2 and 4 normal. Interradiary: variations in gyri 1, 2, 4 normal, other two scanty and degenerate; No. 5 worst. Radii: ditto. Vascularity and chrome + in all in different degrees and varying intensity, even in same gyrus.

Summary.—The tangential layer is the worst, next superradiary. In some gyri they and interradiary are normal. Radii: also only degenerate in minority. Variations in different gyri for all fibres. The same gyrus worst in all. Vascularity and chrome +, and follow fibre-changes in the main.

Sulci.—Much as gyri; in some fibres degenerate, in others sound. Vascularity and chrome +.

Central "B" (another part, 5 gyri).—Tangential fibres: degenerate as a whole, not always scanty. No. 1 not degenerate. Variations in different gyri and parts of individual gyri. Superradiary: ditto. Interradiary: normal, and good Baillarger. Radii: three normal, two degenerate and scanty. Vascularity and chrome +, with variations, as for fibres.

Summary.—One gyrus normal throughout. The two outermost layers are affected equally, with variations as described. Radii: more affected than interradiary. Vascularity and chrome follow fibre-changes. Perpendicular fibres appear in the best gyri.

Sulci.—One normal; others show fibre-degeneration in two outermost layers. Vascularity and chrome + in varying degree.

Summary of central.—The two outermost cross-layers show degeneration, with variations in degree as described; the tangential sometimes the worst; in rest they are equally affected. The interradiary are principally normal, and more so in one part of the region than the other. The radii normal in majority of gyr, but quite as much affected as interradiary. Vascularity and chrome +, and follow fibre-degeneration. Most sulc show degeneration of fibres, especially of outermost layers, and vascularity and chrome +.

Parietal near occipital "A" (6 gyri).—Tangential fibres: very scanty and very degenerate in all; some gyri worse than others. Superradiary: ditto, and some gyri worse. Interradiary: ditto. Radii: Vascularity and chrome greatly +, and in association. All fibres worst near the chromo-vascular patches. No perpendicular fibres.

Summary.—All medullated fibres very degenerate and equally, the same gyri being worse in all respects. Vascularity and chrome +, with fibre-changes.

Sulci.—Fibres very degenerate, especially two outermost layers; superradiary worst. Vascularity +, also chrome, but less so.

Parietal near occipital "A¹" (same part, 7 gyri).—Bears out the preceding.

Parietal near occipital "B" (another part, 7 gyri).—Tangential fibres: scanty and degenerate in all. Superradiary: extremely scanty and degenerate in all; worse than tangential. Interradiary: very scanty and very degenerate in all. Baillarger persists more than others. Radii: very scanty and very degenerate throughout; some more than others. Vascularity greatly + throughout. Chrome +, but with variations. All fibres worse near vascular and chromy patches. No perpendicular.

Summary.—The cross-layers are very degenerate throughout, and so are the radii, though not so consistently, as there are variations. Superradiary: worse than tangential, and interradiary quite as bad as latter. The greater persistence of Baillarger is to be noted. Vascularity and chrome are greatly +, but not always associated.

Sulci.—Fibres degenerate, especially outermost two layers, sometimes absent. Vascularity and chrome +. Inflammatory patches occur.

Summary of parietal near occipital.—Great degeneration of cross-layers and radii, with some variations in different gyri. The superradiary is sometimes the worst layer. Vascularity and chrome greatly +, and the nerve-fibres are worst in association with the areæ of vascularity and chrome. Perpendicular fibres partake in the general degeneration. Baillarger's layer shows greater persistence than rest of interradiary fibres. The sulci show similar conditions as to fibre, vascularity and chrome; the two outermost layers are the worst.

Occipital near tip "A" (9 gyri).—Tangential fibres: normal in four gyri, degenerate in others, with variations between gyri, and locally in individual gyri. Superradiary: same; normal in same and most in same, with variations as above. Interradiary: ditto. Radii: ditto. The worst fibres are in connection with engorged vessels and chrome patches. Perpendicular fibres: worst in worst gyri. Genuari's band is good in the best. Many strong fibres in normal parts. The gyri with best fibres are not vascular; others are unduly vascular and vary. Chrome in excess in all but two gyri; very variable distribution.

Summary.—The cross-layers less degenerate than in preceding areæ, being normal in four out of nine gyri. In the degenerate gyri variations occur, as above described. Same remarks apply to radii. Genuari's band strong and perpendicular fibres present in good specimens. Vascularity and chrome +, and follow fibre-degeneration, the latter less regularly.

Sulci (12).—Five normal as regards fibres and vascularity and chrome. Rest show degeneration, especially of outermost two layers; vascularity and chrome +, irregularly distributed.

Occipital near tip "B" (another part: 9 gyri).—Tangential fibres: three normal, others moderately degenerate;

summit of gyri worse, and variations between and in gyri. Superradiary: five normal, including above three; remainder moderately degenerate, with variations. Interradiary: normal throughout. Radii: normal in seven; others moderately degenerate. Vascularity +, goes with fibre-degeneration. Chrome +, with vascularity, but less regular distribution. Perpendicular fibres: thin and scanty.

Summary.—The cross-layers are less degenerate than in previous specimens, including occipital "A"; only outermost two layers affected, and tangential worse. Variations in degree, as above. The radii affected in limited degree. Vascularity and chrome +, chiefly with fibre-degeneration.

Sulci.—Normal, except two. In these only tangential fibres affected. Vascularity = + in both.

Summary of occipital.—The cross-layers and radii are less degenerate than in former parts of the brain examined, and less in some parts of the occipital than in others. Several normal gyri. Variations in degree of degeneration exist in the affected gyri and in different parts of individual gyri. Superradiary less affected than tangential, in some cases never more affected. Interradiary layer normal, and radii practically the same. Vascularity + with fibre-degeneration, and chrome also, but more irregular distribution.

Sulci.—Much as gyri; several normal, others show degeneration, especially of outermost two layers. Vascularity and chrome as in gyri.

Temporal "A" (7 gyri).—Tangential fibres: very scanty and extremely degenerate; two gyri show variations in degree within the gyrus. Superradiary: very scanty and very degenerate; variations between and in gyri. Interradiary: ditto. Radii: ditto. Vascularity and chrome + in all, chiefly in deeper parts

Summary.—Cross-layers and radii everywhere very degenerate, with variations in different gyri, and within gyri. Vascularity and chrome +, and go with degeneration. Perpendicular fibres very scanty and degenerate.

Sulci (6).—Vascularity and chrome +. Fibres of outermost two layers degenerate in all, and interradiary ditto in three.

Temporal "B" (another part: 7 gyri).—Tangential fibres: extremely scanty and extremely degenerate. Variations between and in gyri, summit worst. Superradiary: ditto. Interradiary: ditto. Radii: scanty, very degenerate. Vascularity and chrome +. Perpendicular fibres thin and tortuous.

Summary.—A very bad specimen. Extreme degeneration of cross-layers, and radii is not much better. Variations in degree, as in last; but this specimen is worse than temporal "A."

Temporal "B" (same part: 7 gyri).—The same conditions as the last. Superradiary fibres are the worst. Sulci as in last.

Summary of temporal.—Extreme degeneration of cross-layers and radii, with variations in different and in individual gyri. Vascularity and chrome +, in association with fibre-degeneration. The conditions are worse than in occipital region, and worse in some parts of temporal than in others. The sulci rather less affected, the two outermost layers chiefly. Vascularity and chrome +.

General summary.—In this case of paralytic dementia of the "florid" type there is widespread and marked degeneration of all the cortical medullated fibres. The anterior portion of the frontal lobe and the mid-temporal region show the most marked degeneration, and one appears to be as bad as the other. Next comes the parietal near the occipital, thereafter the frontal near the descending frontal, then the central, and lastly the occipital region, with moderate degeneration and several normal gyri. Some parts of a region or lobe are worse than another, and variations in degree of degeneration between different, and even between different parts of individual, gyri are noticed. The two outermost layers are often the worst, sometimes equally bad, sometimes one, sometimes the other, worse. There is an absence of strong and of perpendicular fibres in the worst parts, whereas in the normal gyri they are present. Baillarger's band is also noted in normal gyri, with a greater persistence than other interradiary, in some gyri where the interradiary are involved in degeneration. The radii on the whole follow the cross-fibres in degeneration, being worst where latter are worst, and *vice versâ.* But in the frontal region they are not so notably degenerated as in the temporal. In the least affected (central and occipital) they are mostly normal, and not extremely affected where diseased. Of vascularity and chrome it may be said that they are greatly increased, the vascularity being often enormous, and they vary directly with the degree of fibre-degeneration. Fibres are commonly worst in connection with foci of vascularity and chrome. The sulci show fibre-degeneration and increase of vascularity and chrome, usually much in same degree as the gyri with which they are associated. The absence (destruction) of Meynert's external association fibres (with the outermost layers) in the sulci of frontal specimens is striking, as this is very uncommon.

(20) A. W.—On admission: mania. Causation: heredity alone assigned. Clinical course: continued mania with much eroticism, passing into chronic mania which, with superadded mental weakness, was present at death. Cause of death: pneumonia. Total duration: 30 years. Age at death: 73.

Frontal (*pre-central*) "*A*" (6 gyri).—Tangential fibres: scanty, moderately degenerate throughout, with variations in different gyri and in individual ones. Superradiary: scanty and degenerate in all; similar variations. Interradiary: scanty and degenerate; two worse than others. Radii: normal in two, degenerate in varying degrees in others. Vascularity and chrome +, together with variations in different gyri. Perpendicular fibres degenerate; Baillarger fibres not distinguishable.

Summary.—Cross-fibres show moderate degeneration. Radii less generally affected. Variations in degree of degeneration. Vascularity and chrome +, with same variations.

Sulci (5).—Fibres moderately degenerate. Vascularity slight on the whole. Chrome increased in some.

Pre-central "A" (same part: 6 gyri).—Bears out previous specimens. No perpendicular and no Baillarger fibres observed.

Summary pre-central.—See under "A."

Parietal "A" (4 gyri).—Tangential fibres: rather scanty and moderately degenerate; some strong ones; variations in different and in individual gyri. Superradiary: ditto. Interradiary: two normal, with strong fibres; others scanty and moderately degenerate. Baillarger band good. Radii: moderately degenerate and rather scanty. Vascularity = 0 in three, + in one. Chrome + in three.

Summary.—The two outermost cross-layers worst, but only moderately degenerate. Variations as described. Interradiary less affected, but radii as much. Vascularity not increased in general, but chrome is.

Sulci (4).—Fibres mostly degenerate. Normal in one. Vascularity = 0; chrome +.

Parietal "B" (another part: 3 gyri).—Tangential fibres: scanty and degenerate, with variations as described in last. Superradiary: one normal, others very scanty and degenerate. Interradiary: two normal, the third degenerate. Baillarger layer good where fibres normal. Radii: same as interradiary. Vascularity = 0; chrome +, moderately and interradiary. Perpendicular fibres numerous and moderately degenerate.

Summary.—The cross-fibres and radii show degeneration, moderate; the two outermost layers more uniformly, and tangential most so. Vascularity = 0; chrome moderately and locally +.

Sulci.—Fibres scanty and degenerate. Vascularity and chrome = 0.

Summary parietal.—The cross-fibres and radii are moderately degenerate, especially two outermost layers, with variations in different and in individual gyri. A rather better specimen than the pre-central. Vascularity is not increased; chrome moderately so.

Sulci.—Fibres mostly scanty and degenerate. Vascularity and chrome not increased.

Occipital "A" (15 gyri).—Tangential fibres: normal in six; degenerate to moderate extent, and with variations between and in gyri in nine. Superradiary: normal in seven; moderately degenerate in eight, with same variations. Interradiary: normal in four; moderately degenerate and scanty, with variations, in eleven. Radii: normal in six, in nine scanty and moderately degenerate, with variations. Vascularity + in all save two. Chrome + moderately. Variations as in fibre-degeneration. Perpendicular fibres normal.

Summary.—The cross-layers and radii are normal in a large number of gyri and show only moderate degeneration in the others. No one layer worse than another. Variations in degree of degeneration, including local variations in individual gyrus, in all layers. Vascularity and chrome are +, especially former, with the same variations. Perpendicular fibres not affected.

Sulci.—Majority show scanty and degenerate fibres with vascularity and chrome +. Only one normal one.

Occipital "A^1" (same part, 11 gyri).—Tangential fibres normal in nine gyri, the other two show extreme degeneration in patches, in connection with vascularity and chrome. Superradiary: eight normal, the rest as in tangential fibres. Interradiary: same as superradiary. Radii: ditto. Vascularity and chrome normal in three, in eight they are +, with variations in different gyri.

Summary.—Greater part of specimen is normal; the two diseased gyri show extensive degeneration, all layers equally involved. Vascularity and chrome are +, out of proportion to the fibre-degeneration. Perpendicular fibres moderately degenerate.

Sulci (11).—Five normal. Others show fibre-degeneration and patchy vascularity and chrome.

Occipital "A^2" (same part, 7 gyri).—Tangential fibres normal in four, the others moderately degenerate, with variations between and in gyri. Superradiary: ditto. Interradiary: two normal, and others also except for foci of fibre-degeneration in connection with vascularity and chrome. Radii: five normal, others show local degeneration as above. Perpendicular fibres moderately degenerate, Genuari's band only prominent in one gyrus. Vascularity and chrome + in six, chiefly patchy, and variations in gyri, as above.

Summary.—More widespread, though moderate, degeneration amongst cross-layers than in last. Some gyri normal. Radii principally normal. The degeneration is chiefly focal, in connection with vascularity and chrome. Variations in degree as described.

Sulci (4).—Fibres degenerate, interradiary least. Vascularity and chrome +.

Summary of occipital "A."—Only moderate degeneration of cross-layers and of radii in equal measure, and many gyri normal. Degeneration chiefly focal, in connection with vascularity and chrome +, in patches.

Sulci.—Fibres degenerate: fewer normal than *sulci.* Vascularity and chrome +.

Occipital "B" (another part: 5 gyri).—Tangential fibres normal, except for focal degeneration in connection with increase of vessels and connective tissue. Variations in gyri. Superradiary: normal. Interradiary: ditto in three, foci of degeneration in others. Radii: ditto. Vascularity and chrome +, in patches. Gyri four and five worst in all respects.

Summary.—Moderate degeneration of cross-layers and of radii in foci, with increase of vascularity and chrome: apart from these the specimens are normal.

Sulci (2).—Fibres degenerate and vascularity and chrome +.

Summary of Occipital.—The cross-layers and radii are normal in a large number of the gyri examined, but in about an equal number there is moderate degeneration, all layers being about equally involved. Variations in degree of degeneration between gyri and in gyri. The chief feature is the focal degeneration in connection with increase of vascularity and chrome in patches.

Sulci.—More show degeneration (of moderate degree) than in case of gyri. Vascularity and chrome +.

Temporal (7 gyri).—Tangential fibres extremely scanty and degenerate in all, with similar variations to last. Superradiary: three normal, four degenerate and scanty. Interradiary: all normal. Good Baillarger. Radii: ditto. Vascularity and chrome + slightly, with variations in different gyri.

Summary.—The two outermost cross-layers show degeneration, the outermost being the worst and most widespread. Varations in degree of degeneration as described. Vascularity and chrome slight, probably because the deeper parts are normal.

Sulci.—Fibres normal. Vascularity and chrome only slight.

General Summary.—In this case of chronic mania the cross-layers are only moderately degenerate in the different regions examined, the pre-central area being the most affected, thereafter the parietal, followed by temporal and occipital regions. In the occipital there are several normal gyri. The two outermost layers are commonly most affected, without notable distinction. The radii are involved as much as the interradiary. Throughout the layers there is a disposition for fibre-degeneration to be present in foci associated with increase in vascularity and chrome. Variations in degree of degeneration are present between gyri and parts of individual gyri. Perpendicular fibres are only moderately degenerate, with the rest of the fibres.

Sulci.—Are quite as degenerate, in respect to fibres, as the gyri, and rather fewer are normal. Vascularity and chrome are only slight.

(21) M. E.—On admission: acute mania. Causation: third attack (no cause given for previous attacks)—this one stated to be due to worry and the puerperal state. Clinical course: she passed from mania into melancholia, and gradually became stuporose. At death: melancholia with stupor. Cause of death: phthisis. Total duration: 5¼ years. Age at death: 37.

Frontal.—Tangential fibres: extremely scanty and very degenerate. Superradiary: ditto. Interradiary: worse than above. Radii: scanty, degenerate. No perpendicular fibres. Vascularity = 0, chrome +. in patches.

Summary.—Cross-layers very scanty and degenerate; interradiary the worst, and superradiary the next. Radii participate. Vascularity = 0. Chrome +.

Parietal "A."—Tangential fibres: not scanty, moderately degenerate. Superradiary: ditto. Interradiary: normal. Radii: ditto. Vascularity and chrome = 0.

Summary.—Moderate degeneration outermost, two layers.

Parietal "A" (same part).—As in last. Some perpendicular fibres exist. Vascularity = 0. Chrome +, irregularly.

Temporal.—Tangential fibres: numerous, moderately degenerate. Superradiary: very scanty and degenerate; worse. Interradiary: moderately degenerate, fairly numerous. Variations in degree of degeneration in the gyrus. Radii: ditto. Perpendicular: very scanty and moderately degenerate. Vascularity = 0. Chrome +, general and in patches of intensity.

Summary.—Moderate degeneration of cross-layers and radii, with variations, superradiary excepted, these the worst. Vascularity = 0. Chrome +.

Occipital "A."—Tangential fibres: very scanty and very degenerate on summit: normal elsewhere. Superradiary: ditto. Interradiary, degenerate, but less so. Radii: trunks normal, terminals degenerate over summit. Vascularity = 0. Chrome +, worse in patches.

Summary.—Cross-layers degenerate, but only over summit. Two outermost layers worst, and terminals of radii involved.

Occipital "B" (another part).—Tangential fibres: scanty and degenerate, except on one side, where they are normal. Superradiary: more locally affected. Interradiary: very scanty and degenerate on one side, normal elsewhere. Radii: ditto. Vascularity = 0. Chrome greatly +.

Summary.—A worse specimen than last; all layers show degeneration, tangential most, others equally, with much variation in individual gyrus, normal parts adjoining diseased. Vascularity = 0. Chrome much +.

Summary of Occipital.—Cross-layers show moderate degeneration, also radii, but only in parts of the individual gyri, and some parts of the area are worse than others. No vascular increase, but chrome is +.

General Summary.—In this case of emotional disorder the cross-layers show varying degrees of degeneration in different parts, the frontal specimens being the worst, with marked degeneration of all layers, temporal, occipital and parietal, following in order the last has only the outermost two layers affected. In the occipital considerable variations exist within the limits of the individual gyrus. The tangential sometimes, sometimes superradiary, is worst. In the frontal specimen the interradiary is worst—an unusual condition. Radii most affected in the frontal and temporal, following cross-fibres. Vascularity is not increased with fibre-changes, whereas chrome is—an unusual condition. The perpendicular fibres, as far as noted, follow the others in point of degeneration.

(22) D. L.—On admission: delusions of persecution. Causation: heredity only assigned. Clinical course: the state persisted for some five years, then dementia became more apparent. At death dementia with mild delusions. Total duration: 37 years. Cause of death: pneumonia.

Frontal "A."—Tangential fibres: scanty and degenerate. Superradiary: worse, very scanty and very degenerate. Interradiary: worse: extremely scanty and very degenerate. Radii: scanty and degenerate; terminals worse. Vascularity and chrome = 0. No Baillarger band.

Frontal "B" (another part).—Much as above, only tangential shows variations. Some degenerate perpendicular fibres.

Summary.—Marked degeneration of cross-layers, interradiary worst, superradiary next. Terminals of radii equally bad. Baillarger not present, and perpendicular fibres degenerate. Vascularity and chrome = 0.

Parietal "A" (2 gyri).—Tangential fibres: extremely scanty and very degenerate in one; numerous; moderately degenerate in other. Superradiary: normal in places, very degenerate at others; summit degenerate. Interradiary: normal in one, scanty and degenerate at summit in other. Radii: moderately degenerate in one, great degeneration in other. Vascularity = 0. Chrome +, only at sides.

Summary.—Cross-layers (especially two outermost) and radii show degeneration, the latter as much as the former, with marked variations between neighbouring gyri. Vascularity = 0. Chrome +, regularly.

Parietal "B" (another part : 1 gyrus).—Tangential fibres: extremely scanty and very degenerate. Superradiary: rather less affected. Interradiary: slightly scanty and slightly degenerate. Radii normal. Vascularity and chrome as in last.

Summary of Parietal.—All cross-layers degenerate, tangential worst; superradiary next. One specimen shows local variations, the other does not. Radii show quite unlike conditions in the two specimens. Vascularity does not follow fibre changes, but chrome is increased. One sulcus; much same conditions as gyri; the two outermost layers of fibres affected.

Occipital "A" (2 gyri). — Tangential fibres: fairly numerous; moderately degenerate. Superradiary: normal; many strong fibres. Interradiary: ditto. Radii: ditto. No vascularity. Chrome +. Some perpendicular fibres.

Summary.—A normal specimen, except for moderate tangential degeneration. One sulcus: normal.

Occipital "B" (another part: 2 gyri).—Same description as for last. Chrome is +, and general. One sulcus: normal.

Temporal "A" (2 gyri).—Tangential fibres: very scanty and very degenerate. Superradiary: worse. Interradiary: very scanty and moderately degenerate. Radii: very degenerate. Vascularity is slight. Chrome general, and also increased in patches.

Summary.—All cross-fibres and radii show considerable degeneration, the outermost layers chiefly, superradiary most. Vascularity not proportionately increased. Chrome is +. One sulcus; same conditions as gyri.

Temporal "B" (another part).—The same description as for last. One sulcus: the same.

General Summary.—In this case of delusional insanity, with terminal dementia, the cross-layers show marked scantiness and degeneration in frontal and temporal regions to about an equal extent. The parietal region is less affected, and the occipital is normal, except for moderate tangential degeneration. A point is that the interradiary layer is sometimes worst and sometimes the superradiary. The tangential is not oftener the worst. No local variations, except in parietal. In the two worst regions the radii show considerable degeneration, but less in the parietal. Vascularity is not increased, notwithstanding the fibre-degeneration (and that the case died from pneumonia). Chrome is generally +, and therefore does not follow vascularity. In the very degenerate frontal no Baillarger band is made out, and the perpendicular fibres are degenerate. Sulci follow gyri, showing much the same degenerations in the degenerate parts, and being normal in normal parts.

(23) H. L.—On admission: subacute mania. Causation: senility +, a previous attack (33 years before, lasted 12 months). Clinical course: the same state until death. Total duration: two months. Cause of death: chronic renal disease and brain atrophy. Age at death: 66.

Frontal "A" (7 gyri).—In six gyri, tangential fibres, superradiary and interradiary, normal, but some degeneration of fibres observed in the two latter layers about foci of vascularity and chrome. Radii: normal. Baillarger well marked. Some perpendicular fibres noted. In gyrus 7 all fibres scanty and moderately degenerate; parts of the gyrus worse than others. Vascularity + in all; chiefly superradiary and interradiary Chrome + and around the vessels.

Summary.—Cross-layers and radii normal in six out of seven gyri, except in connection with areæ of vascularity. No. 7 is degenerate. Vascularity and chrome +.

Sulci (7).—In four, fibres are normal; in three, scanty and degenerate. Vascularity and chrome +.

Frontal "A" (same part: 8 gyri).—The same conditions as in "A."

Frontal "B" (another part: 13 gyri).—Tangential fibres normal in eleven gyri, except for moderate degeneration in connection with congested vessels. In Nos. 12 and

13 they are scanty and very degenerate; worst in 12. Superradiary: ditto. Interradiary: ditto. Radii: normal in nine, except about vessels; in two others only the terminals degenerate at summit; in 12 and 13 the radii very degenerate. Vascularity + in all, worst in 12 and 13. Chrome +, follows vessels.

Summary.—Cross-layers and radii normal in eleven gyri out of thirteen, except for moderate degeneration in connection with vascular disturbances. They are very degenerate in the two remaining gyri. Vascularity and chrome + in all, but worst in last-mentioned gyri.

Sulci.—Outer two layers moderately degenerate in all except two, where fibres are normal. Vascularity and chrome irregularly increased.

Frontal "B" (same part, 13 gyri).—The conditions are the same.

Summary of frontal region.—The cross-layers and radii are normal in the great majority of gyri, except where they abut on foci of vascularity and chrome.

In the minority of gyri the medullated fibres are either moderately or, at times, very degenerate, with occasional variations in degree in individual gyri, and vascularity and chrome are more marked in these. The sulci show moderate fibre-degeneration, with vascularity and chrome +; but many sulci are normal.

Parietal "A" (in or immediately behind ascending parietal: 7 gyri).—Tangential fibres: five gyri show degeneration, No. 1 being worst; variations in individual gyri in respect of degeneration; two gyri normal, except where fibres trench on congested vessels. Superradiary: three gyri show degeneration, to which above applies; four are normal, with similar reservations. Interradiary: two show moderate degeneration, as above; five normal, similarly. Baillarger and perpendicular fibres well marked in some. Radii: only one gyrus shows degeneration. Vascularity +; chrome + only in the most vascular gyrus, No. 7.

Summary.—The tangential fibres show the most widespread degeneration, the condition being more limited as one proceeds from without inwards; radii only affected in one gyrus. Even in the normal gyri there are degenerate fibres about the congested vessels in all layers. Variations in intensity of degeneration, as described. Vascularity +, but chrome generally not so.

Sulci.—Fibres normal in majority, and vascularity and chrome are +.

Parietal "A^1" (same part: 8 gyri).—Tangential fibres: scanty and very degenerate in all. Superradiary: very scanty and very degenerate. Interradiary: ditto. Baillarger exists only in two. Radii: degenerate; variations in different gyri. Vascularity +; chrome = 0.

Sulci.—Fibres degenerate, and vascularity and chrome + in all, some worse than others.

Summary.—A much worse specimen than last, though taken very near it. All cross-layers very degenerate, and radii involved, though to a less degree. Vascularity +; chrome = 0.

Parietal "A^2" (same part: 6 gyri).—Same summary as in last; vascularity + in all; chrome = 0, except in one gyrus.

Sulci (9).—Fibres throughout very scanty and very degenerate, especially outermost two layers. Vascularity and chrome +.

Parietal "A^3" (same part: 8 gyri).—Tangential fibres: normal in all, except No. 8; these very degenerate, especially at summit. Superradiary: ditto. Interradiary: ditto. Baillarger band well marked; some perpendicular fibres. Radii: ditto. Vascularity + in all, except one gyrus; worse locally in individual gyri; worst in No. 8. Chrome +; worst in No. 8. Three gyri free.

Summary.—A much better specimen than last. Medullated fibres normal in all, except in one; here very degenerate, especially at summit. Vascularity +, out of proportion to fibre-changes, but most marked where latter worst. Chrome much the same, but less widespread.

Summary of parietal.—There are great variations in the state of the medullated fibres in different sections; in some sections only the tangential fibres show consistent degeneration, in others, taken very near the last, all fibres show great degeneration in all gyri. In others, again, all fibres are normal. In respect to all otherwise normal gyri a reservation is made as regards foci of fibre-degeneration in all layers in connection with vascularity. Baillarger's band and the perpendicular fibres are found in the most normal gyri. Vascularity is +, chiefly as large, isolated, congested vessels, and follows fibre-changes. Chrome does not regularly follow vascularity, and is often absent. The sulci follow gyri approximately; those connected with better sections have normal fibres, and *vice versâ.* Vascularity and chrome are +.

Parietal posterior to ascending parietal "A" (8 gyri).—Tangential fibres: scanty and moderately degenerate in all. Superradiary: ditto; in most gyri worse than tangential. Interradiary: scanty and moderately degenerate; no Baillarger. Radii: scanty and moderately degenerate. Vascularity + greatly in foci. Chrome +, around vessels. A few degenerate, perpendicular fibres. Seldom variations in individual gyri.

Summary.—The cross-layers and radii are throughout degenerate, chiefly in moderate degree, but superradiary are the worst. Baillarger absent, perpendicular fibres degenerate. Vascularity and chrome + in foci; large blocked vessels.

Sulci.—Vascularity and chrome + in all and fibres scanty, except in one normal specimen; but vascularity is + in this also.

Parietal posterior to ascending parietal "B" (another part: 7 gyri).—Tangential fibres: scanty, moderately degenerate. Superradiary: ditto. Interradiary: slightly degenerate and scanty. Baillarger more marked in some than others. Radii: normal except in one, where moderately degenerate and scanty. Vascularity +, but chiefly capillary. Chrome is slight. Strong fibres very rare.

Summary.—A better specimen than last, the two outermost layers only being equally affected. Vascularity and chrome are also less.

Sulci.—As in gyri.

Summary of parietal posterior to ascending parietal.—The appearances differ in different parts, one being more degenerate than the other. Degeneration is usually moderate. Superradiary region in places the worst. Interradiary not always better than tangential. Baillarger band and perpendicular fibres affected in more degenerate parts, and vascularity and chrome greater.

Sulci.—These in general show less degeneration. Vascularity and chrome +.

Occipital "A" (far back in the lobe, near tip: 7 gyri). Tangential fibres: scanty and moderately degenerate in all, chiefly on summit. Gyri differ in degree, and individual gyri show differences, parts normal and others degenerate. Superradiary: ditto. Interradiary: normal. Radii: ditto. Vascularity and chrome + in association in all. Strong fibres in fair amount in all layers.

Summary.—The two outermost layers show moderate degeneration, with variations as described. Vascularity and chrome +.

Sulci.—Fibres normal. Vascularity + in all and chrome in some.

Occipital "B" (another part, more forward: 9 gyri).—Tangential fibres and superradiary: scanty and moderately degenerate in six gyri; in rest of gyri all fibres normal. Baillarger well marked in some. Vascularity and chrome +, as in last.

Sulci (6): normal; a capillary vascularity.

Summary.—Much the same conditions as in "A."

Occipital "B" (same part: 9 gyri).—Same conditions as last.

Summary of occipital.—But little fibre-degeneration, only the outermost two layers showing it in moderate and equal degree. Variations in degeneration in parts as described. Vascularity and chrome + in association. Baillarger fibres and strong, are not affected. The sulci are less affected, vascularity only being moderately increased; no fibre-changes.

Temporal "A" (4 gyri)—Three normal. In fourth: tangential fibres: moderately degenerate. Superradiary:

ditto. Interradiary: ditto. Radii: extremely degenerate. Vascularity + in all, chiefly interradiary, worst in fourth. Chrome + in all, but less in fourth.

Summary.—Normal in greater part except for increase in vascularity and chrome. One gyrus shows moderate degeneration of cross-layers and much greater of radii. Vascularity and chrome +, though former alone follows fibre-degeneration.

Sulci (3).—Superradiary: fibres degenerate in one, and vascularity and chrome +.

Temporal "A[1]" (same part, 10 gyri).—Tangential fibres: six are normal and four others also except for scantiness and moderate degeneration at summit. Superradiary: ditto. Interradiary: nine normal, one very degenerate. Baillarger's band in many of the normal. Radii: normal in eight, and in other two only terminals degenerate. Vascularity and chrome + in all, chiefly interradiary.

Summary.—Cross-fibres and radii normal in the main, the outermost two layers showing moderate degeneration at summit in a minority. One very degenerate gyrus as regards interradiary. Vascularity and chrome +.

Sulci (7).—Normal except for moderate degeneration in connection with vascular patches.

Temporal "A[2]" (same part: 4 gyri).—Tangential fibres: scanty and degenerate and worst at summit in three, normal in one. Superradiary: ditto. Interradiary: normal. Radii: normal in two, in others scanty and moderately degenerate, especially at summit. Vascularity and chrome +, chiefly interradiary.

Summary.—The two outermost cross-layers moderately degenerate, with local variation, in majority of gyri. Interradiary: normal, whilst radii moderately involved in some gyri. Vascularity and chrome +.

Sulci (3).—Fibres normal. Vascularity and chrome +, with variations between sulci.

Summary of temporal "A."—Moderate degeneration of cross-layers, especially outermost two, in minority of gyri. Variations in degree of degeneration in individual gyri frequent. Radii: less affected, but to a greater extent than cross-fibres in one gyrus; one very degenerate interradiary layer also seen. Baillarger's band in many of them normal. Vascularity and chrome – uniformly, and in association. Sulci show also only moderate degeneration of fibres in connection with patches of vascularity and chrome.

Temporal "B" (another part, 6 gyri).—Tangential fibres: normal in five, scanty and moderately degenerate over summit in sixth. Superradiary: three normal, others scanty and moderately degenerate. Interradiary: normal, except one, where the fibres moderately degenerate over summit. Baillarger hardly exists. Radii: fibres and terminals degenerate, especially at summit in Nos. 1 and 2; four are normal. Vascularity and chrome + in all, with variations in different and in individual gyri, chiefly interradiary.

Summary.—Cross-fibres not free from moderate degeneration, though this is very limited, most gyri being normal. The superradiary most widely degenerate. Interradiary not better than tangential, and radii are as much involved as either. Vascularity and chrome +, rather out of proportion to fibre-changes.

Sulci (5).—Fibres chiefly degenerate. Vascularity and chrome + in all with variations.

Temporal "B" (same part, 9 gyri).—In seven, tangential fibres are normal; moderately degenerate and scanty, chiefly at summit in two. Superradiary: normal in all. Interradiary: ditto. Radii: ditto. Perpendicular fibres fairly numerous and normal. Vascularity and chrome + in all, chiefly interradiary.

Summary.—Normal conditions with slight or very localised tangential degeneration in two. Vascularity and chrome also disproportionately increased.

Sulci (7).—Fibres normal, but vascularity and chrome greatly +.

Summary of temporal "B."—Very limited and moderate degeneration of cross-fibres and of radii. The gyri are chiefly normal. One specimen rather worse than the other, although cut from very near latter. Perpendicular fibres normal. Vascularity and chrome +, and out of proportion to fibre-changes.

Sulci.—These agree with the gyri in presenting moderate fibre-degeneration, not widespread, and vascularity and chrome +, out of proportion to this.

Summary of temporal.—The cross-layers are only moderately and very locally degenerated, the majority of the gyri being normal. The radii on the whole are less affected, but in rare instances as much and even more. Variations in degree of degeneration in individual gyri: often only a very limited part involved, rest of gyrus normal. Baillarger's band and perpendicular fibres noted in many of the normal. Vascularity and chrome − generally and often out of proportion, as stated.

Sulci.—Only moderate degeneration, where affected: largely normal. Vascularity and chrome +, general.

General summary.—In this case of subacute mania the degeneration of the cross-layers and radii is very seldom striking, a large number of gyri being normal throughout the hemisphere, and only moderate degeneration, as a rule, occurring where any is present. Throughout there is an increase in the fibre-degeneration locally in connection with patches of vascularity and chrome. Here the impression left is that the vascular changes wêre initial and those of the fibres secondary; the vascular patches are often very prominent, composed of large blocked vessels, whilst the fibre-degeneration is, as a rule, moderate. And outside these foci the fibres are so frequently normal; and the general vascularity is often out of proportion to the changes in fibres. Some very degenerate sections are in close proximity to others nearly normal. In one region (hind-parietal) it is noted that the superradiary layer is often the worst: otherwise the two outermost layers are on the whole the most affected, though superradiary is as much involved as tangential, and fairly often the interradiary layer is as involved as either.

Variations in degree of degeneration occur frequently between gyri and parts of individual gyri. Baillarger, strong, and perpendicular fibres are noted as well marked where gyri are normal, and absent or degenerate and scanty in some of the worst specimens. In the frontal, central, and parietal regions the radii show moderate degeneration in several gyri, the terminals being worse; less in temporal region. In the occipital they are normal. Vascularity and chrome are generally +, and go together with fibre degeneration, though vascularity is in some areæ + out of proportion thereto. Foci of large, blocked vessels, with deep chrome-areæ about them, occur. There is no marked difference in degree of degeneration between the different parts of the hemisphere: the central and paretial regions are rather the worst, and frontal is no worse than occipital and temporal; the latter three about equally involved.

Sulci.—Are chiefly like the gyri, showing normal condition of fibres usually, and only moderate degeneration where any. Vascularity and chrome are +, and out of proportion to fibre-changes

(24) R. M.—On admission: acute mania; much incoherence; hallucinations; no violence. No cause known (a vagrant). Clinical course became quieter, but remained hallucinated and deluded and very incoherent. Able to work. This was the condition at death, which was due to pneumonia. Age at death: 27. Total duration: 5—6 years.

Pre-central (9 gyri).—Tangential fibres: very scanty and very degenerate. Some variation in gyri; in the worst they are practically absent. Superradiary: ditto. Interradiary: less scanty, but almost as degenerate; no Baillarger. Radii: very scanty and very degenerate. Variations between gyri, in respect of these and last. Vascularity +, generally, chiefly capillary. Chrome +, but less regularly, and not always following vascularity. In No. 9 chrome obliterates all fibres, except tangential. No perpendicular and no strong fibres.

Summary.—Great degeneration of cross-layers of radii. Tangential and superradiary worst and equally affected. Occasional variations between gyri. Vascularity +, diffuse. Chrome +, but less regularly, and not always with vascularity. In great excess in one gyrus.

Pre-central "A^2" (9 gyri, same part).—The same conditions.

Sulci (9).—Fibres very scanty and very degenerate on the whole, with fewer variations than on gyri. Vascularity and chrome + and together.

Parietal "A" (2 gyri).—Tangential fibres: abundant, moderately degenerate. Superradiary: scanty, moderately degenerate. Interradiary: normal. Good Baillarger. Radii: normal, terminals moderately degenerate. Perpendicular fibres: very scanty and moderately degenerate. Strong fibres in various layers. Vascularity +, large blocked. Chrome +.

Summary.—Moderate degeneration of the outermost layers, in which terminations of radii involved.

Parietal "B" (another part; 2 gyri).—Tangential fibres: very scanty and very degenerate; worse in one gyrus. Superradiary: ditto. Interradiary: very scanty and extremely degenerate in one gyrus, and Baillarger absent; the other less affected but still scanty and degenerate. Radii: in both degenerate; terminals worse. Vascularity + in both. Chrome + in both. Both less in one gyrus. Perpendicular fibres scanty; strong fibres not marked.

Summary.—Great degeneration of all cross-layers, interradiary equally with others, with variations between gyri. Radii involved, but less so, except terminals. Vascularity and chrome +, with variations as above.

Summary of parietal.—Great variation in degree of degeneration of fibres; moderate of two outermost layers (with terminals of radii) in one part; extreme of all layers, with radii involved, in the other. Strong, perpendicular, and Baillarger fibres better in the better specimen. Vascularity and chrome general, and +.

Temporal (4 gyri).—Tangential fibres: extremely scanty and very degenerate in three, less in fourth. Superradiary: less scanty, with variations in different gyri; very degenerate; summit worst. Interradiary: numerous, very degenerate. Baillarger well marked. Radii: moderately degenerate, terminals worse. Vascularity + in all. Chrome = 0 in two, except about vessels; dense in two. Strong fibres, few, degenerate; perpendicular fibres = 0.

Summary.—All cross-layers show much degeneration, progressively less from without inward; radii less affected, but terminals equally with cross-fibres. Majority of gyri equally affected. Vascularity + uniformly; chrome irregularly +.

Occipital "A" (8 gyri).—Tangential fibres: very scanty in five, numerous in three; very degenerate in all save seven and eight, these only slightly so. Superradiary: scanty in six, numerous in two, and very degenerate; only slightly so in seven and eight. Interradiary: scanty and moderately in three, normal in three (including Nos. 7 and 8), numerous and moderately degenerate in two. Baillarger only present in "numerous" ones. Radii: moderately degenerate, terminals worse; in Nos. 7 and 8 only terminals affected. Vascularity greatly + in all; chrome only slight. Perpendicular fibres: few and degenerate.

Occipital "B" (another part, 7 gyri).—The same conditions.

Summary of occipital.—The outermost two cross-layers chiefly affected, usually scanty, and commonly very degenerate in equal degree. Terminals of radii equally involved; other fibres in less degree. Two gyri much better than others. Vascularity +; chrome only slight.

Sulci (4).—Fibres degenerate. Vascularity and chrome as above.

General summary.—In this case of acute passing into chronic mania there is considerable degeneration of the cross-fibres, especially of the two outermost layers, and in equal degree in all regions, the frontal being the worst, the parietal and temporal about equally involved, and the occipital least. The radii are almost as affected as the cross-fibres in the frontal, but less in the others, though their terminals are always involved. Strong and perpendicular fibres are absent in the worst specimens. Variations between gyri and in individual gyri in the less degenerate specimens. Vascularity is consistently +, and is probably in association with the pneumonia, which caused death; but chrome does not regularly follow.

The sulci show much the same conditions as the gyri.

(25) M. B.—On admission: acute mania. Causation: no assigned cause, the condition came on as simple mania, and this produrmal state lasted 2 years. Clinical course: the simple mania passed into an acute condition which lasted 2 months, thereafter acute delirium supervened, lasting 6 weeks, about. Great emaciation; sordes; syncopal attacks. She died in one of these. Cause of death: exhaustion from acute mania: Brown atrophy of the heart. Age at death: 31.

Frontal (3 gyri).—Outermost zone is occupied by chrome and capillaries, obliterating the tangential fibres. All cross-fibres extremely scanty and extremely degenerate. The radii are also very scanty and very degenerate, scarcely less so than the others. Vascularity + general but not marked. Chrome is moderate, except in anterior zone. No perpendicular, no Baillarger, and no strong fibres.

Summary.—An exceedingly degenerate specimen.

Parietal (2 gyri).—Tangential fibres obscured by chrome and capillaries. Superradiary: very scanty and very degenerate in one, not so far gone in the other. Interradiary: scanty: some largeness: very degenerate. Radii very scanty and very degenerate. Vascularity and chrome = 0, except in outermost layer. No Baillarger fibres; perpendicular fibres rare and degenerate.

Summary.—A very degenerate specimen, not quite so bad as frontal.

Occipital (3 gyri).—The fibres are scanty and degenerate throughout, including the radii. No Baillarger band. Some perpendicular and strong fibres exist, but are degenerate. Vascularity = 0. Chrome = intense in outermost zone, and large patch occurs on one side of gyri, tending to obscure all layers.

Summary.—A very degenerate specimen, rather less so than the two preceding.

Temporal (3 gyri).—Tangential fibres: a very few degenerate to be seen, most of the zone obscured by chrome. Superradiary: scanty, but less so than in previous; extremely degenerate. Interradiary: ditto. Radii: ditto. Some degenerate, strong and perpendicular fibres seen throughout. Vascularity = 0. Chrome slight, except for outermost layer.

Summary.—A very degenerate specimen, but on the whole the least of all.

General summary.—In this case of acute mania passing into acute delirious mania the cross-layers and radii show very great degeneration in all parts examined, the frontal gyri being the most affected, the temporal least. The tangential fibres cannot be made out, except very rarely, owing to deposit of chrome and to capillary engorgement in the outermost zone. The pia only moderately thickened. The other cross-fibres are about equally affected, and the radii are but little less involved, the degeneration in all fibres being extreme. The perpendicular fibres, the strong and the Baillarger disappear in the worst gyri, and are very scanty and degenerate in the others. Notwithstanding fibre-degeneration the vascularity and the chrome—apart from the outermost zone—are very slight.

The conditions as to *vascularity* and *chrome-deposit* in the various cases examined may be summarised as follows: —In 13 out of the 25 cases—and in various forms of insanity, mostly those of some years' duration—the vascularity is considerably increased, commensurately with the degree of fibre-degeneration. The increase is chiefly in the interradiary and superradiary layers. It is most marked in the cases of paralytic dementia (although these are of comparatively short duration). In 4 of the 13 cases there was a bodily disease, causing death (pneumonia 3, Landry's paralysis, 1), which might have been regarded as responsible for the cortical congestion; but in two other cases in which pneumonia caused death there was no such congestion. And in other cases dead of phthisis the vascularity was increased, though anæmia might have been looked for. Therefore it is fair to assume that the vascular congestion in the above-mentioned four cases was connected with cortical disease, as manifested by the fibre-changes.

In four cases in which the fibre-degeneration was considerable or extreme, the mental disorder having lasted in some a few weeks, in others several years, vascularity is only slight, not commensurate with nerve-fibre changes. In seven others, under similar conditions, it is even entirely absent. These eleven cases embrace instances of acute and chronic insanity. In one case of subacute mania (two months' duration, death from chronic renal changes), without marked fibre-degeneration, the vascularity and chrome-deposit are increased out of proportion to latter.

Chrome-deposit (often exceedingly deep) is generally associated with increased vascularity, but does not follow fibre-degeneration quite so closely. [This deposit in the specimens must be associated with a morbid change in the tissue. The most diseased gyri show it most. Its presence cannot be explained by faulty technique.]

General Conclusions.

(1) In seventeen out of twenty-five cases marked and widespread degeneration of the medullated fibres of the cortex was observed. In six of these this was extreme, as follows:—One case of delusional insanity (6 years' duration); one dementia paralytica, maniacal type (2 years); one ditto (5½ months); one puerperal insanity, with variations in emotional state (5¼ years); one acute mania, passing into acute delirium (4 months); one acute mania (1¾ years).

In three others of the twenty-five cases there was considerable degeneration, but more locally; slighter degeneration in general. The remaining five cases showed moderate degeneration.

In some cases of paralytic dementia there was great variation in degree of degeneration between sections cut very near each other in the same piece (whole piece not above 8-9 mm. in depth).

(2) Atrophy of fibres can be more extensive and intense in cases of a few months than in those of many years' duration.

(3) The pre-central region (frontal lobe) showed the most degeneration in nine out of twenty-three cases (in two remaining it was not examined), and was equal to the worst region in four others. In only one case was this the least

affected area. Next followed the temporal region; worst in four, equal to worst in two. The centro-parietal region is least affected in eight, the majority of instances, and is worst only in one case.

The fibre-degeneration is often quite as marked in other parts as in the frontal region, and sometimes more so.

The occipital lobe is not spared in general paralysis of the insane as Tuczek stated; this statement Zacher has already denied.

(4) As regards the cross-layers: the tangential and superradiary are the worst and earliest involved, and are equally affected in the majority of cases. The superradiary rather than tangential is oftener the worst. As the latest development of the "primary" fibre-deposit, the superradiary might be expected to be earliest involved. In three cases only are the three layers equally affected. The interradiary is commonly less involved, seldom as much, very rarely is worse. These conclusions are at variance with Tuczek's findings for general paralysis of the insane.

(5) The radiations are less affected than the cross-fibres in eleven cases, equally, or nearly so, in eleven, and equally locally (in certain parts) in three. They are never worse than the cross-fibres. The terminals of the radii are always worse than the trunks, where the radii are involved, and are often involved where the trunks are normal. They share equally in the degeneration of the superradiary fibres.

(6) Variations in degree of degeneration between neighbouring gyri, and also between parts of individual gyri, are frequent in the less diseased parts.

(7) The "strong" fibres and the "perpendicular" ones are very generally very degenerate or absent in specimens showing disease, whilst still degeneration is only moderate in the bulk of the cross-fibres. It is interesting to recall in this connection that the former are regarded as a later development than the latter.

(8) There is considerable increase in vascularity (congestion: sometimes more than this) in thirteen cases, commensurately with fibre-degeneration, and slight increase (non-commensurate) in four others. The increase is most

marked in the cases of paralytic dementia. Absence of vascularity in a few acute cases with great degeneration of fibres is notable.

(9) Chrome-deposit is often extreme, especially in the most diseased gyri, and generally in association with increased vascularity (about the vessels); but does not follow fibre-degeneration quite so closely as does vascularity.

(10) The fibre-degeneration in the sulci is, on the whole, equivalent to that in the adjoining gyri, as far as the outermost two layers are concerned. The interradiary fibres but seldom show disease. Vascularity and chrome are commonly similar to the conditions obtaining in the adjoining gyri.

DESCRIPTION OF FIGURES.

FIG. 1.—Normal medullated fibres. × 25.

FIG. 2.—Parietal cortex from a case of acute puerperal mania. Normal, except for slight degeneration of superradiary layer (not seen under this magnification). × 35.

FIG. 3.—To show general paucity of the cross-fibres. From a case of paranoia. × 35.

FIG. 4.—Sclerosis of outermost cortical layers (aniline blue-black, fresh section). For comparison with fig. 5. × 65.

FIG. 5.—A section from same part as fig. 4 (corresponding). Showing persistence of tangential fibres in fair number notwithstanding the sclerosis of outermost zone shown by the fresh method in fig. 4. Chronic mania. × 65.

FIG. 6.—Showing scantiness and degeneration of the radii and interradiary fibres, especially varicosities. Chronic melancholia; dementia. × 300.

FIG. 7. Showing great paucity of all fibres, vascularity and chrome-infiltration, and patches of sclerosis in outermost zone. Acute melancholia. × 65.

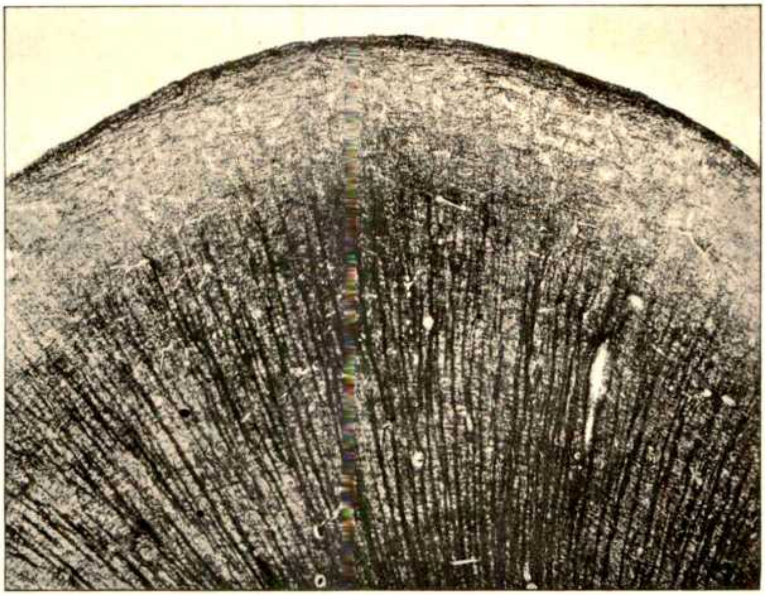
FIG. 8.—Destruction of medullated fibres, vascularity, chrome-infiltration. Paralytic dementia. × 25.

FIG. 9.—Same conditions as last. Same case. × 25.

FIG. 10.—Tortuosity of the radiations. Paralytic dementia. × 300.

FIG. 11. -Foci of vascularity and chrome. The fibres only moderately diseased. × 35 (but somewhat higher magnification required to show the superradiary). Subacute mania.

FIG. 12.—Extreme destruction of fibres, including radiations; fibres almost entirely absent. Greatly increased vascularity and chrome-infiltration. Paralytic dementia. × 35.



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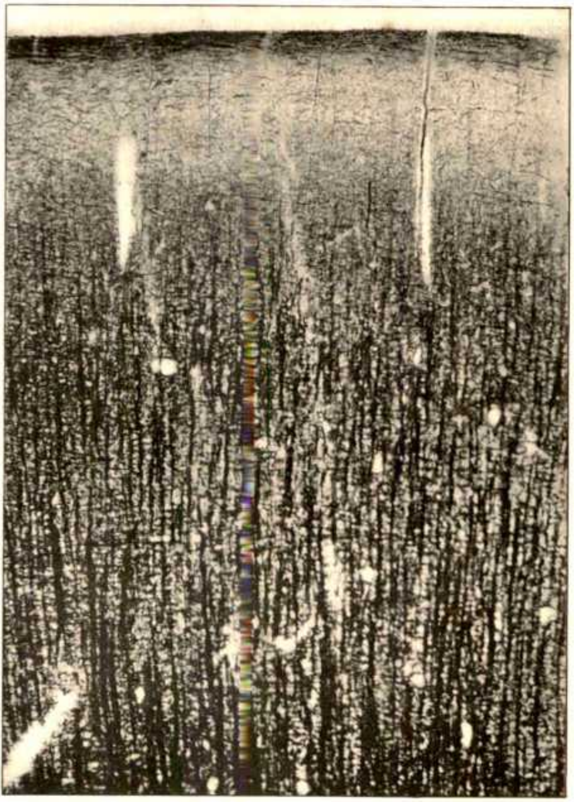

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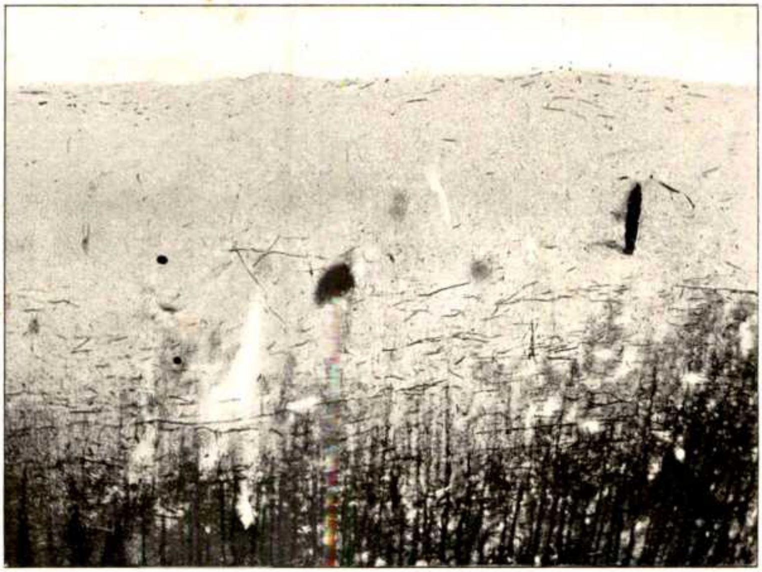

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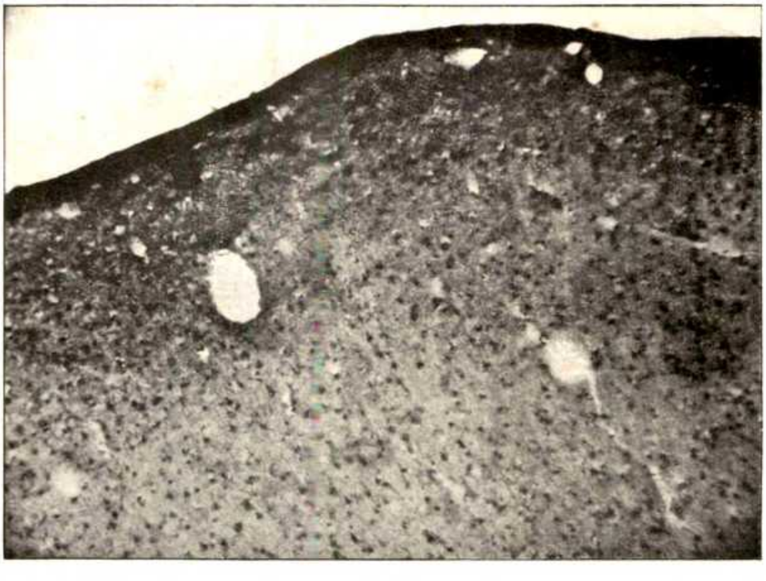

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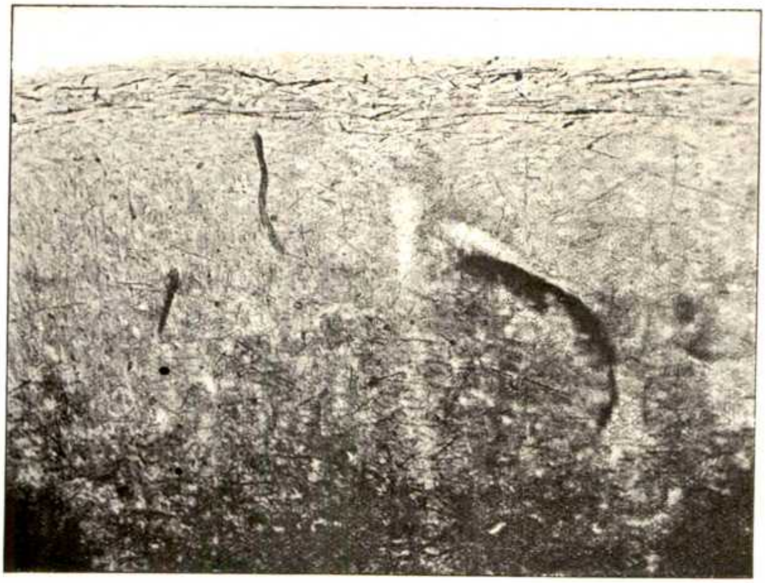

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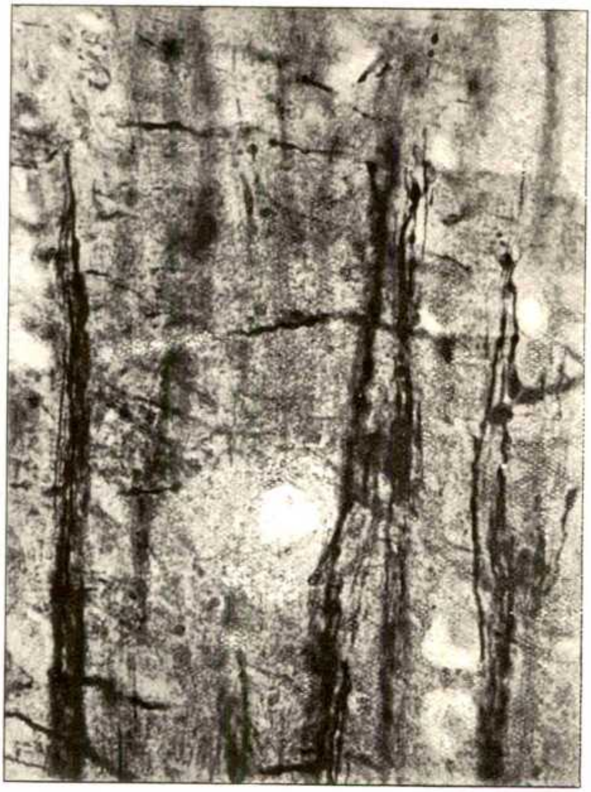

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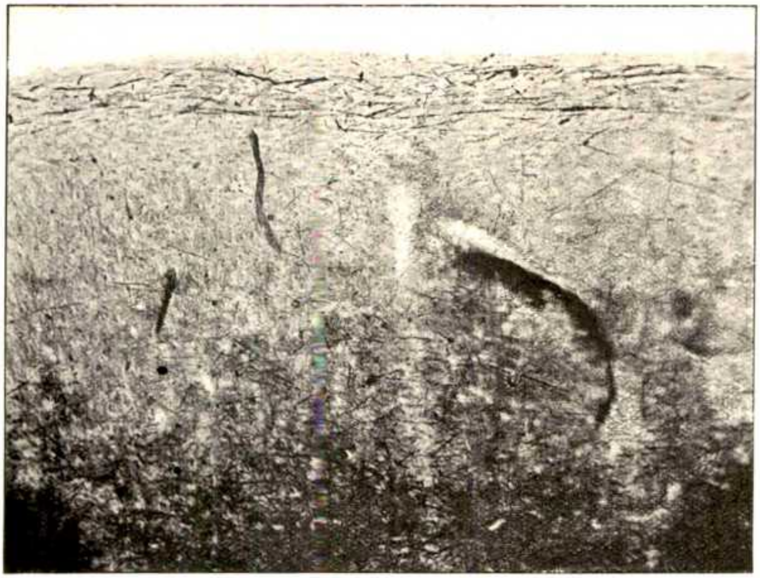

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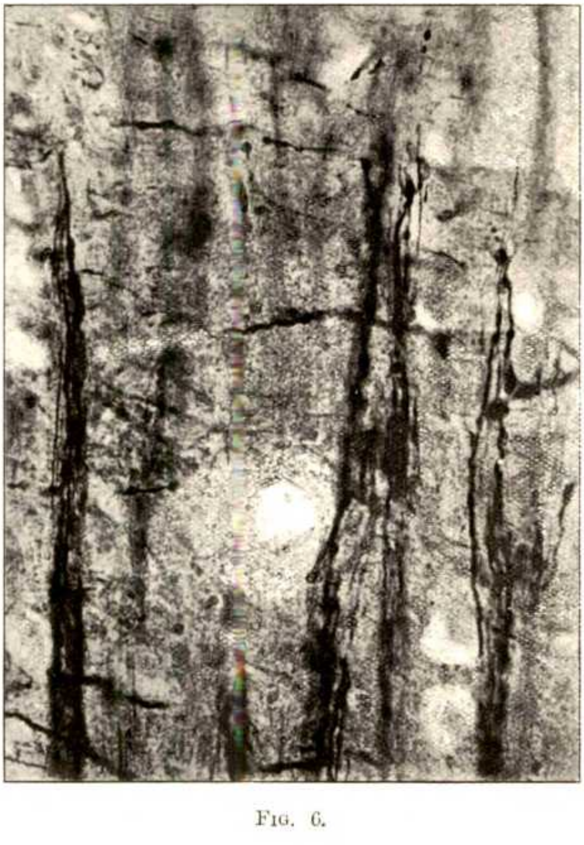

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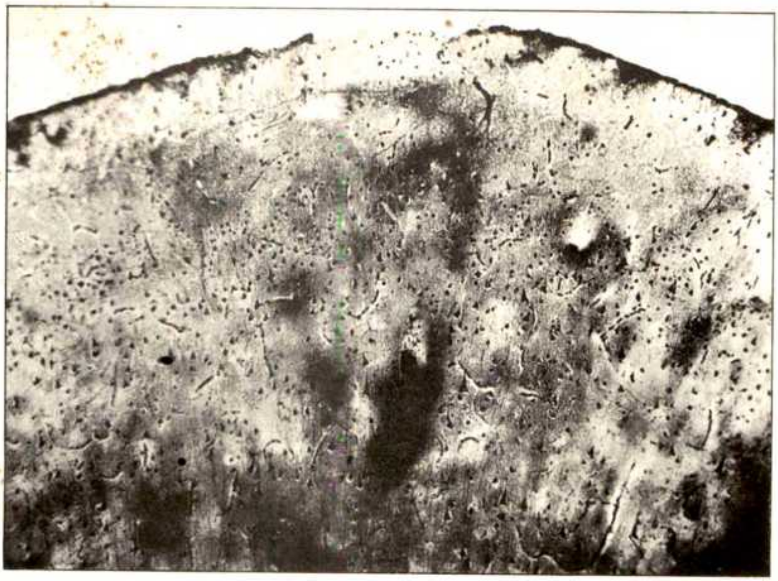

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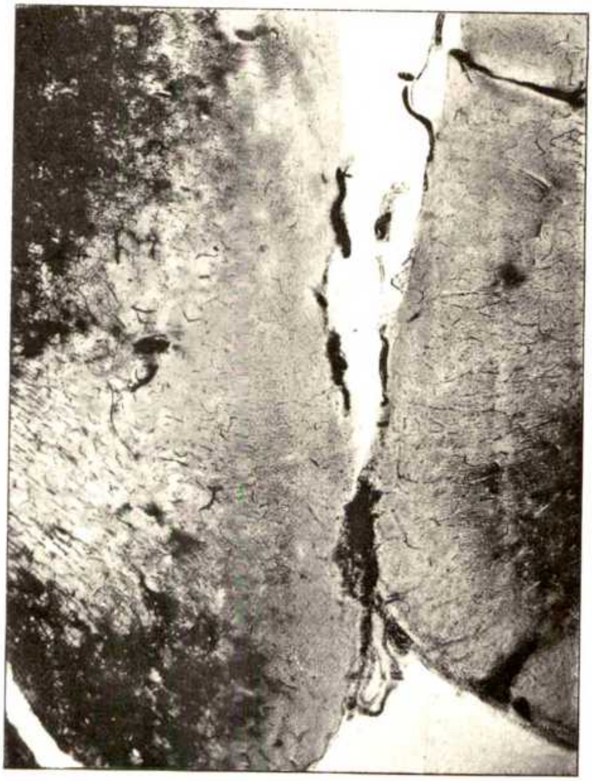

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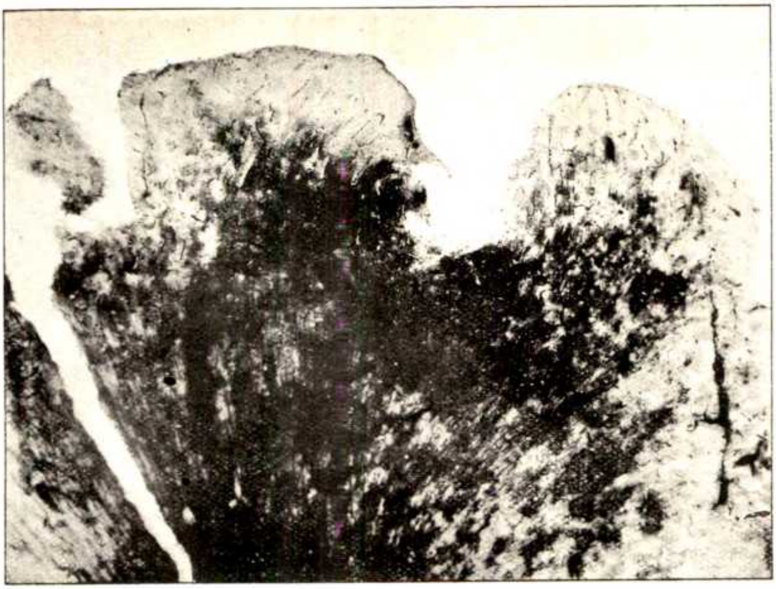

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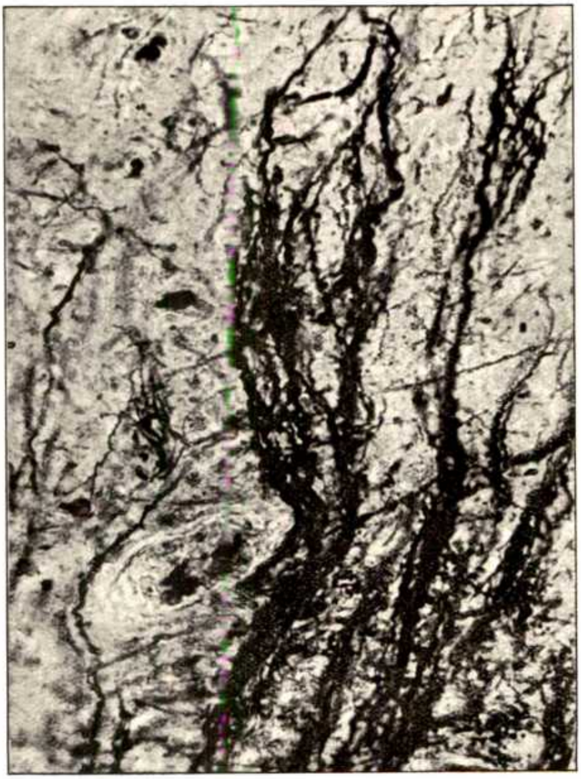

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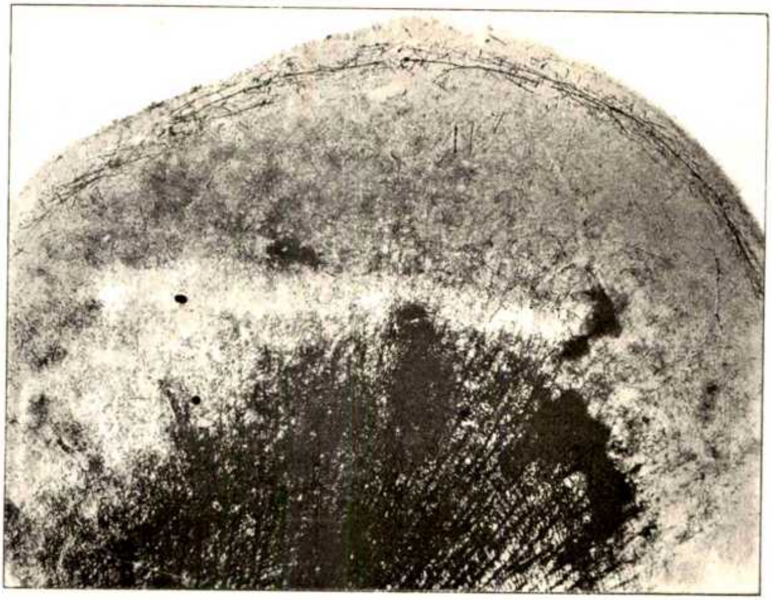

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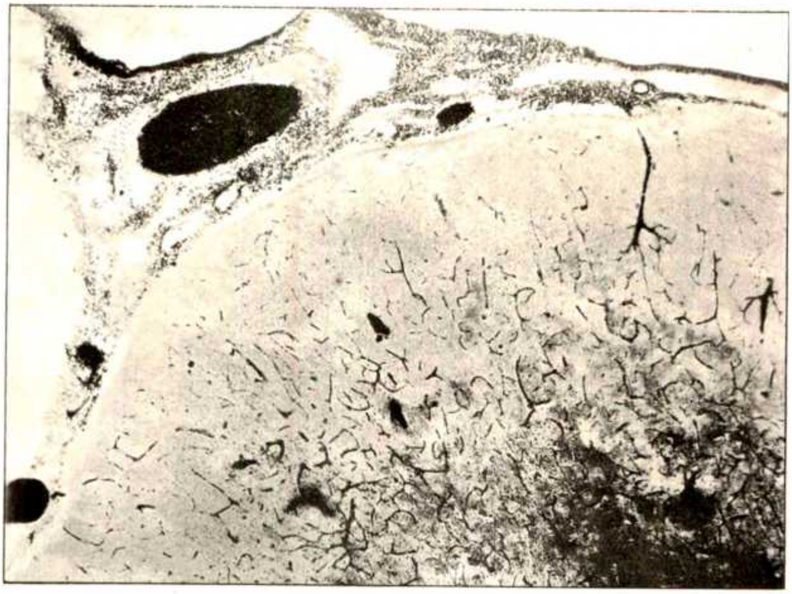

FIG. 12.

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OBSERVATIONS ON THE COURSE OF THE OPTIC FIBRES IN A CASE OF UNILATERAL OPTIC ATROPHY.

BY W. B. WARRINGTON, M.D., M.R.C.P.

Demonstrator of Pathology in University College, Liverpool; Assistant Physician to the Hospital for Chest Diseases, and Pathologist to the Stanley Hospital.

AND

J. E. DUTTON, M.B.

Late Holt Fellow in Pathology.

(*From the Thompson-Yates Laboratory.*)

THAT in man a semi-decussation of the optic nerves occurs at the chiasma is almost universally believed; the fact, however, that the veteran histologist Kölliker disputes this position has given a fresh impetus to observations on the question.

Kölliker's position, as described in the last edition of the *Handbuch der Gewebelehre*, is that pure anatomy yields evidence of a complete crossing in man, in the dog and the cat.

His observations were made by serial horizontal sections through the chiasma stained by the Weigert method.

In order to study the course of the fibres a complete series must be made; this is not easy and Kölliker criticises Gudden's original pictures on the ground that they are merely schematic, and that the distinct uncrossed bundle there figured can never be found in nature.

Kölliker (1) has again only last year returned to the subject, and has studied, by means of the Golgi method, the course of fibres in the chiasma of sheep, cats and man. The results he has obtained are that in man it is impossible that any considerable number of fibres pass to the tract of the same side as the optic nerve from which they are derived, though he admits the existence of a very small number of direct fibres.

In addition to this conclusion Kölliker has noticed the important fact that in the cow, cat, rabbit and dog, a division of individual fibres takes place in such a manner that a fibre from one optic nerve passes to the two tracts.

In man Kölliker was only able to find in his specimens one such fibre.

Should further observations demonstrate that division of fibres is a constant occurrence in the chiasma, Kölliker considers this fact would remove in considerable part the physiological objections to his view.

Finally Kölliker urges that the minute anatomy of the chiasma must be more thoroughly observed before the question is settled.

Other authors also favour the view that the decussation is complete, viz., Biesiadecki (2) in 1861, Mandelstamm (3) 1873, Scheel, W. Krause, 1897, and especially Michel (4) 1873-1890.

Mickel maintains:—

(1) That serial sections of the chiasma give no support to the view of semi-decussation.

(2) That investigations of degenerations in man and animals give no evidence of a non-crossed bundle of fibres.

(3) "He argues that if homonymous bilateral hemianopsia is to be explained by the decussation in the chiasma, the proportion of crossed to uncrossed fibres should be as 1·1, and contrasts with this the admission of even those who adhere to the doctrine of partial decussation, that the relation is 3·1, or 4·1, at most as 5·3." (Quoted from Barker, "The Nervous System.")

Our case does not, however, show any marked difference between the amount of degeneration in the two tracts. Further, owing to the limitation of the field of vision, the outer and lower parts of the retina are probably less developed than the inner and lower, and, as Michel himself has found, the number of fibres passing to different sections of the retina is very variable, being least in the outer segment.

Michel also cites the fact that no anatomical evidence has yet been produced demonstrating the double representation of the macula, which is required by the theory of semi-decussation in order to explain the freedom of the fixation point in cases of hemiopia. Michel's hypothesis cannot, however, be regarded as giving a more satisfactory explanation.

Finally Kölliker has been attacked on his own ground by Grützner (5) who, in an admirable critical article, concludes that anatomy can give no definite reply to the question of the complete or partial decussation of the optic fibres. This author made models of the chiasma, in which one half of the fibres were made to cross, the other half to remain on the same side. The models were then embedded in paraffin and cut into a series of horizontal sections. From a study of these sections he states that if he had not been in possession of the actual facts, he would have judged that *all* the fibres were crossed.

In view of the renewed interest which the subject has thus recently attracted we thought it permissible to bring forward the following case of unilateral atrophy of an optic nerve, which shows clearly the existence and arrangement of a semi-decussation in the chiasma, and furnishes also some other points of interest.

Résumé of Case.

Sarah B., aged 63, admitted to the Liverpool Royal Infirmary on January 14, 1898, under the care of Dr. Caton, to whom we are indebted for permission to record the case. Three years previously the patient had received an injury to the right eye, and six months before admission enucleation became necessary and was performed at the Stanley Hospital. On admission to the Royal Infirmary the patient was found to have a greatly enlarged liver. Death occurred in about three weeks after admission, and the autopsy revealed the presence of a large melanotic growth in the liver.

We record here :—

(1) The resulting degenerations in the nerve, chiasma and optic tracts.

(2) The existence of undegenerated fibres in the atrophied nerve.

(3) The condition of the oculomotorius nucleus.

METHOD OF EXAMINATION.

The whole brain was hardened in Müller's fluid, the optic system, with the neighbouring parts of the brain undisturbed, was then removed. By this means it was easy to localise the position of any degenerations that might be found.

The optic chiasma with pieces of each tract and both nerves was removed and placed in Marchi's fluid. The remaining extent of the tracts, with the adjoining brain tissue, including the geniculate bodies and pulvinar, was cut into small sections, 3 mm. in thickness, transverse to the long axis of the tract fibres. These, together with separate pieces of both optic nerves, were also placed in Marchi fluid. The tissues were afterwards embedded in paraffin, cut in serial sections of 10 μ each and then fixed on slides. The chiasma was cut into a complete series of horizontal sections, the remaining parts were cut transversely. As no fibres showed the characteristic Marchi globules they were stained with the acid hæmatoxylin of Schäfer and then treated with Pal's fluids.

This method of paraffin embedding has the advantages that a complete series may be cut, and that the sections are much thinner than can be obtained by the celloidin method. The previous treatment of the tissues by the Marchi fluid enables the hæmotoxylin to stain perfectly well.

I.—*The Resulting Degenerations of the Nerve, Chiasma, and Tracts.*

The naked eye examination of the sections showed that the right optic nerve was completely degenerated, being white and shrunken.

The optic tracts were plainly seen to contain sclerosed tissue, which stood out markedly in contrast to the black-stained nerve-fibres.

Optic nerves.—The left nerve showed the normal structure. The right practically consisted of fibrous tissue; it was very much shrunken and complete atrophy appeared to have taken place.

Careful examination, however, with a $\frac{1}{12}$ in. immersion lens, discovered a few normal nerve-fibres, scattered irregularly over the area of the section. In diameter they never measured more than 1·5 μ, and hence belonged to the smallest of the optic nerve-fibres (see plate, fig. 1).

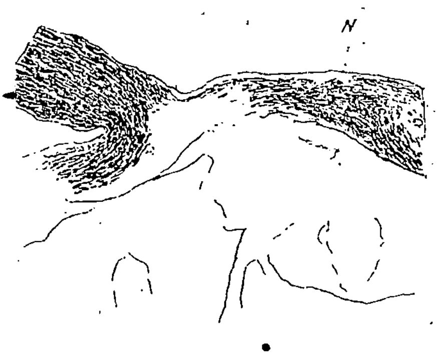
Chiasma.—The chiasma, with the optic nerves attached as described, was cut in a complete series of about 500 horizontal sections, and every fourth one stained. By means of this large number of fairly thin sections, the course of the degenerated tracts could be fairly well traced, and is shown in the accompanying diagrams (figs. 1—5). In the sections about the median plane (figs. 3 and 4 and plate, fig. 4) the atrophy from the right nerve is seen spreading in the central portion of the same-sided tract, and occupying the front and back of the chiasma—its extent being larger in the latter situation.

As the sections approached the upper and lower surfaces the distribution of atrophied tissue was less defined, and the intermingling of normal fibres was greater. The general relations were, however, the same. In looking at figs. 3 and 4 it seems difficult to resist the conclusion that the atrophied tract at B corresponds with the normal fibres at A. The general "grain" of the fibres of the left nerve appear to be sweeping into the left tract, much as the atrophic tissue of the right nerve passes out of the right tract.

Is it possible, despite the observations of Grützner, to rely upon the anatomical evidence?

When we examined this region (*A*) in very thin sections (6 μ) with ocular 4 Zeiss, and $\frac{1}{12}$th inch objective, large strands of fibres cut in longitudinal direction were certainly seen passing in two directions, viz.: (1) streaming through the chiasma; (2) curling round to enter the tract of the same side.

The sections were so thin that the curve on groups of



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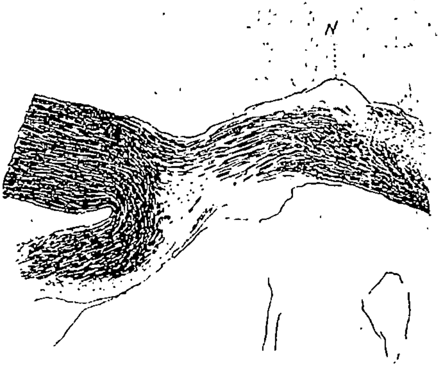

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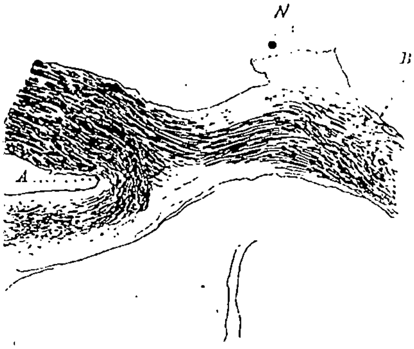

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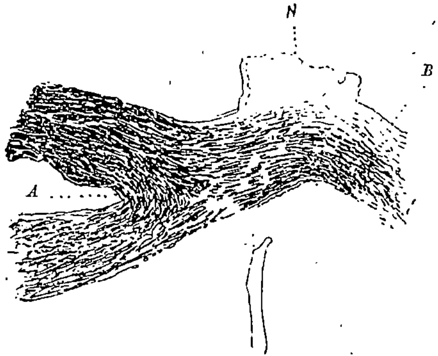

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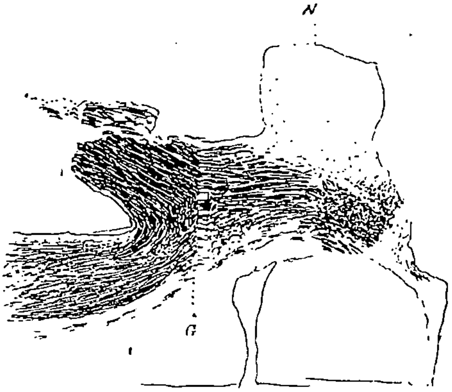


FIG. 5.

FIGS. 1 TO 5.

Series of drawings of horizontal sections of chiasma, made by Edinger's apparatus. Fig. 1 is the most dorsal, fig. 5 the most ventral section.

N = Atrophied right optic nerve.
G = Gudden's commissure.
A = Junction of left nerve with left tract.
B = Junction of right nerve with right tract.

individual fibres could be distinctly seen, and we are inclined to think that the appearance represented an anatomical fact. As pointed out by Michel, the fibres of the optic nerve, as they enter the chiasma, turn sharply at right angles, and again at another right angle when entering the tract of the opposite side. It is this fact which is the cause of the deceptive appearance in anatomical preparation, inclining the observer to believe the fibres enter the tract from the nerve of the same side.

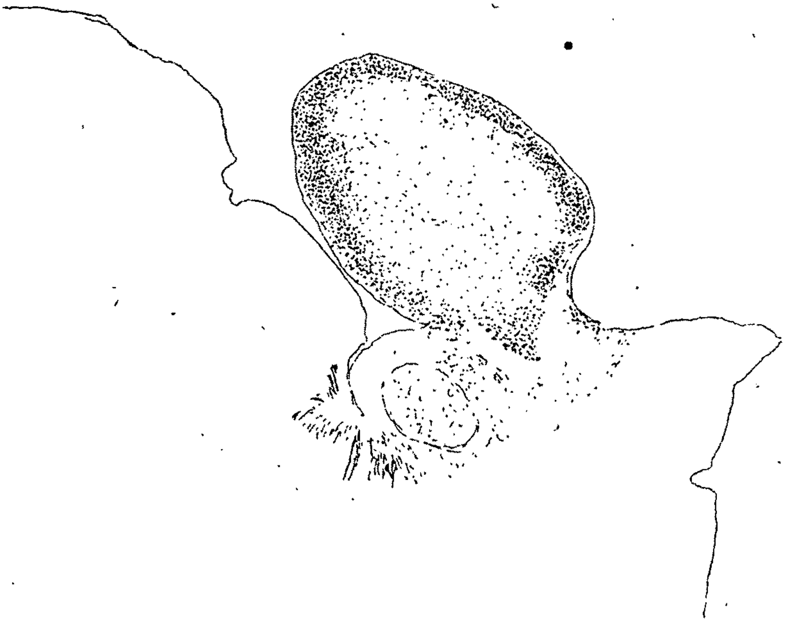


Fig. 6.

Bearing in mind this warning, we are yet of opinion that is not sufficient to explain the appearances alluded to. In these very thin sections groups of fibres having the same direction can be traced along the outer border of the nerve and into the tract of the same side.

Right optic tract.—Sections taken near the chiasma showed that the atrophy occupied a central position extending further outwards than inwards (figs. 6, 7, 8).

Microscopical examination revealed that in no part was there complete atrophy, normal nerve fibres being found in the most affected part of the tract. Many of the normal fibres found in the atrophic tissue were of small diameter (1·5—2 μ), only the minority being as large in diameter as 5—7·5 μ; whereas at the periphery of the section these large fibres greatly preponderated (plate, figs. 2 and 3).

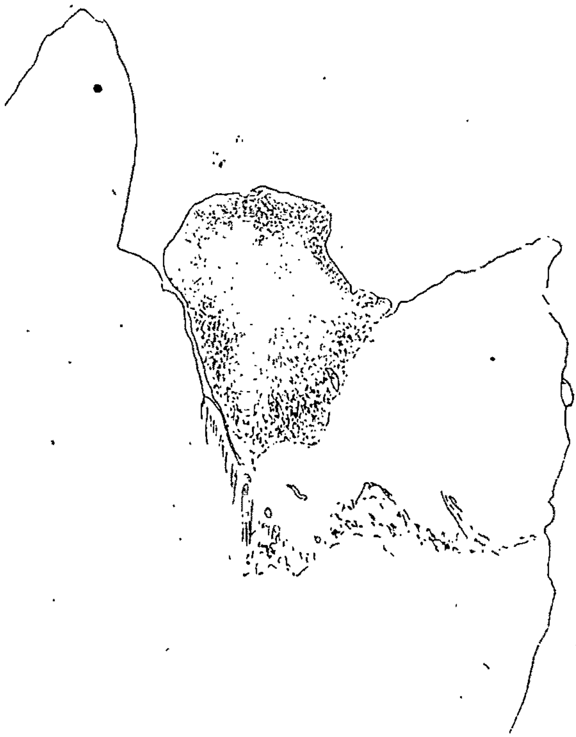


FIG. 7.

The same general distribution was noted in the sections taken from the more centrally situated part of the tract, but the extent of the atrophy gradually diminished.

At the commencement of the level of the external geniculate body no obvious degeneration was seen, but microscopically the fibres on the outer part of the tract

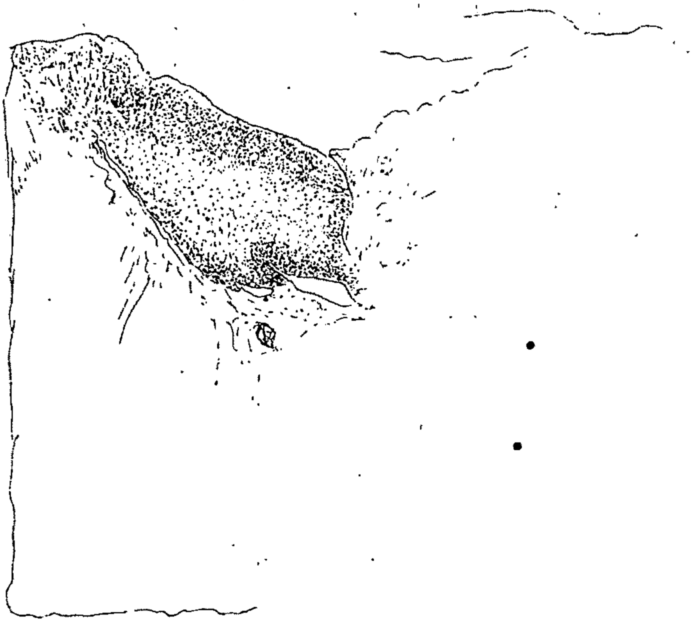
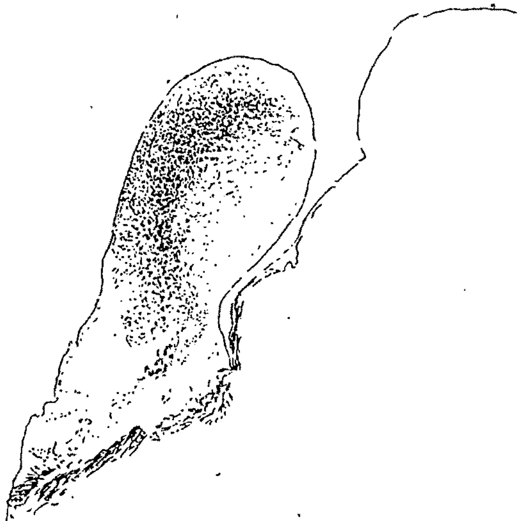


FIG. 8.

FIGS. 6 TO 8.

Series of drawings of transverse sections through the right optic tract. Fig. 6 is nearest the chiasma, fig. 8 near the geniculate body.



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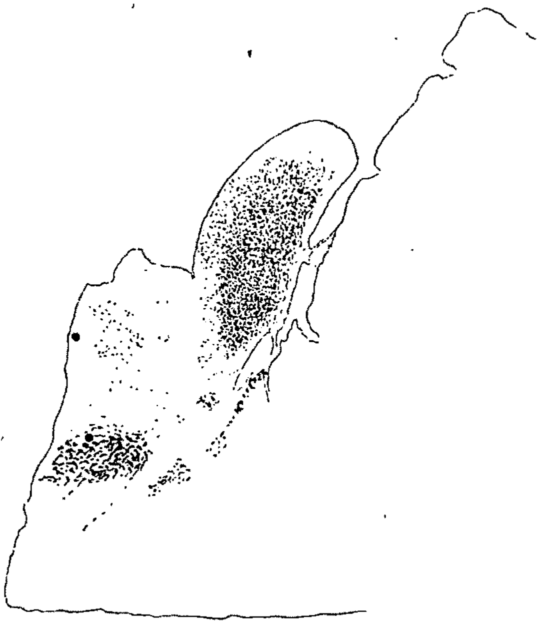

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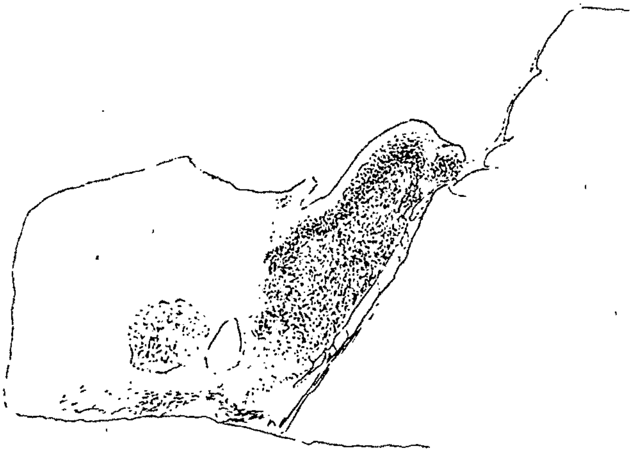

FIG. 11.

FIGS. 9 TO 11.

Series of drawings of transverse sections through the left optic tract. Fig. 9 is nearest the chiasma, fig. 11 near the geniculate body.

were considerably larger and more numerous than those on its inner aspect. Sections through the geniculate body showed that its cellular mass was richly covered by fibres of a large diameter; those deeper in its substance were much smaller.

Left optic tract.—In sections near the chiasma the degeneration is well seen, situated peripherally and chiefly on the inner and inferior aspect of the tract. It is never complete, normal nerve-fibres being present in the connective tissue. Its extent gradually diminishes, as it is traced centrally (figs. 9, 10, 11).

Near the geniculate body the area of degeneration could no longer be observed with the naked eye, but on microscopic examination, the inferior region was found scantily supplied with nerve-fibres.

No obvious difference in size was found between those normal fibres situated in the atrophied region and those composing the undegenerated portion of the optic tract.

REMARKS.

Those who, on anatomical grounds, oppose the prevalent view of a semi-decussation of the optic nerve-fibres, must explain the degeneration appearances in cases similar to ours.

Michel (6) appears to be the only observer who, using the modern methods, has given cases of degeneration and maintained that these support the view of a complete decussation. He mentions and illustrates four such cases which, however, do not appear to us to justify his position; for if, as his figures show, there is no degeneration visible in the tract on the same side as the atrophy—there is only *partial* atrophy in the opposite tract—indeed, as Wieting has remarked, the unprejudiced observer would draw the opposite conclusion to that which Michel does from a study of his figures. The very old observations of Biesiadecki, the more recent ones of Mandelstamm, were made on unstained preparations, and cannot well be compared with Weigert-Pal specimens.

On the other hand, Purtscher (7) records six cases, Wieting (8) three, Siemerling (9) and Williamson (10) one case, stained by the Weigert method, which clearly show the atrophy in both tracts, and in a similar position to that described by us, viz., the crossed fibres occupy the centre of the tract, the uncrossed the periphery. Marchand (11) and Burdach (12) give figures showing clearly atrophy in both tracts, but having a different position.

Hellendall (13) quotes three well illustrated cases showing that the crossed bundle occupied an inner and ventral position in the tract, whilst a triangular field of atrophied tissue was situated just at the commencement of the same-sided tract, which could not, however, be traced any further.

Hellendall and also Hausemann (14), who criticised the cases, considered that the preparation showed also *anatomical* evidence of the existence of uncrossed fibres in the tract on the same side as the normal nerve.

Thus summarising we may state :—

(1) That all observers with the modern methods, with the single exception of Michel, are of opinion that degenerations occur in both tracts after destruction of one optic nerve.

(2) That whilst in general pure *anatomy* cannot demonstrate a decussation, certain cases, *e.g.*, Hellendall's and the present writers', yield some evidence of an uncrossed bundle of fibres.

(3) That the commonest position in which such degenerations in the tracts have been found corresponds to that described above.

II.—*On the Existence of Undegenerated Fibres in the Atrophied Nerve.*

We alluded to the presence of very fine normally-stained fibres in the stump of the atrophied nerve, and to the fact that the fibres remaining in the degenerated portion of the tract of the same side also had an extremely small diameter.

Gudden long ago asserted that the fine fibres of the optic nerve were connected with the anterior corpus quadrigeminum, whilst those of larger diameter could be traced to the geniculate body. Michel very clearly figures similar fibres, Williamson and Wieting also found them, and the latter observer suggested they might be centrifugal in their course.

Hitherto the existence of centrifugal fibres in the optic nerve has been demonstrated by the Golgi method, and their origin could not be ascertained in this way. Recently, however, Wallenberg (15), Boyce and Warrington (16) showed that in the bird a lesion of the optic lobes gave rise to a degeneration extending to the opposite retina. These various observations certainly suggest that the fine fibres may belong to centrifugal neurons, though the evidence adduced is not sufficient to show where their cell origin is.

As shown in the photograph (plate, figs. 2 and 3) the small size of the fibres in the degenerated centre of the tract in comparison with those of the normal periphery is very noticeable, and suggests the possibility that they may belong to the same system as those found undegenerated in the atrophied stump, viz., have a centrifugal course.

III.—*On the Condition of the Oculomotorius Nucleus.*

A series of paraffin sections was made, including the whole of this nucleus, and every fifth section stained by Held's modification of the Nissl method. It is now well known that section of an axis cylinder is followed in general after a short time by the change known as chromatolysis in its nerve cell. Further, that after a considerable period the cells so affected tend gradually to return to their normal condition. In our case the cells of the nucleus were throughout *normal*. It is possible that this repair may have taken place, as observation by Van Gehuchten, Marinesco, and one of us have shown that after a period of 100 days not any very obvious difference is noticeable in any group of cells whose axons have been cut. The application of the law of Nissl for the limitation of a nucleus of origin is not always very satisfactory. Bernheimer (17) and Schwabe (18) have made laborious researches on the connections of the various parts of the oculomotorius nucleus, but their results are not in close agreement. Thus Bernheimer considers that the external muscles of the eye receive in the main a crossed innervation from the nucleus, whilst Schwabe regards the nerve to the superior rectus as alone derived from the opposite side of the nucleus. This author also was unable by this method to locate the nucleus of the internal eye muscles, whilst Bernheimer refers to the cells situated on the lateral part of the nucleus as giving origin to the nerve-fibres which supply these muscles.

In experiments performed by one of us (19), in which the third cranial nerve was divided within the cranium and the oculomotorius nucleus subsequently examined, only changes of a slight nature were found, which were useless for purposes of careful localisation. It is probable that in the case of the eye muscle our efforts should be directed to the localised of cell groups representing combinations rather than single movements.

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The above references are fairly complete as regards cases which have occurred in the human subject. The literature dealing with the general subject is extremely large and is to be found in the works of Gudden, Michel and v. Monakow.

DESCRIPTION OF PLATES.

Photographs taken from sections stained by Schäfer's acid hæmatoxylin method. The black masses represent osmic stain which was not removed by washing. Black rings are normal nerve-fibres.

FIG. 1.

Right optic nerve showing a few undegenerated nerve-fibres in the sclerosed tissue. (Zeiss 3 mm. Apochromatic Oc. 3.)

FIG. 2.

Periphery of right optic tract consisting chiefly of largish fibres. $\frac{1}{5}$ in. obj., Oc. 3.

FIG. 3.

Centre of right optic tract consisting chiefly of small fibres. $\frac{1}{5}$ in. obj., Oc. 3.

FIG. 4.

Section through the centre of chiasma ($5\,\mu$ in thickness).

PLATE.

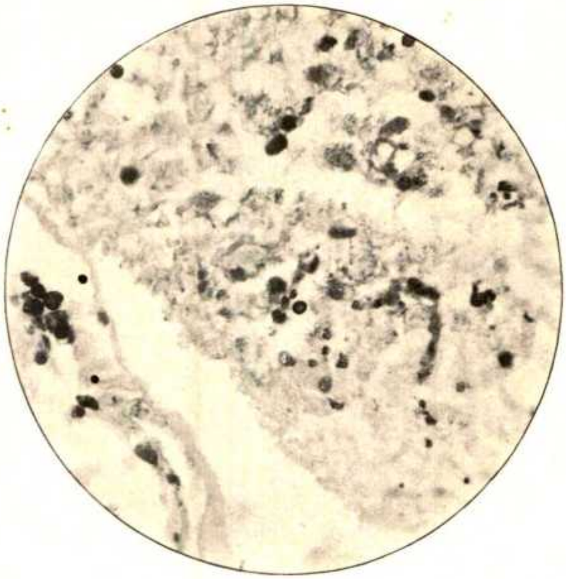

FIG. 1.

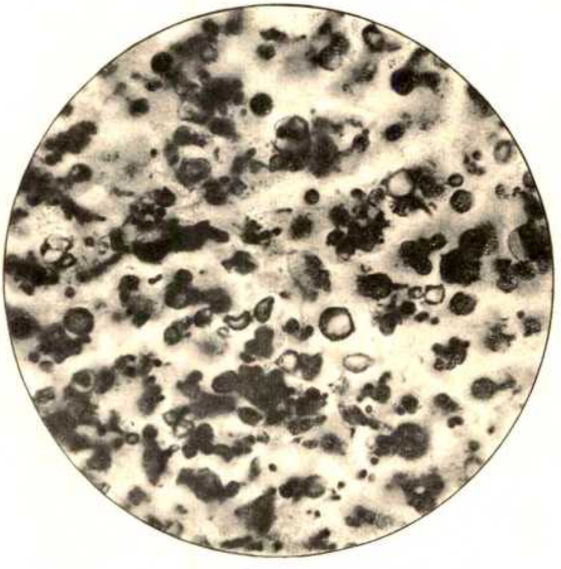

FIG. 2.

PLATE.

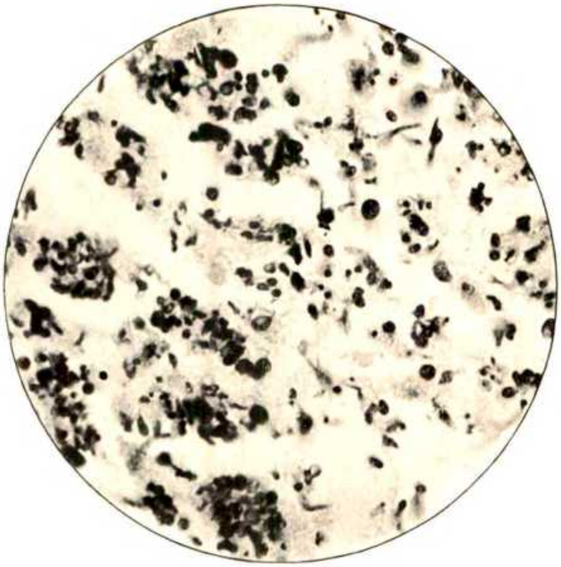

FIG. 3.

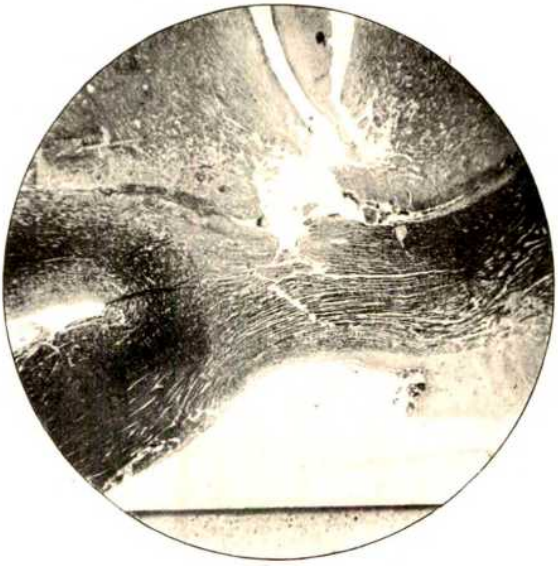

FIG. 4.

CONSIDERATIONS OPPOSED TO THE "NEURON THEORY."

BY ALEX HILL, M.A., M.D.

Master of Downing College, Cambridge.

THE literature of the neuron has been so frequently summed up during the last three years that it would be a waste of space for me to repeat here what is familiar to all neurologists. Dr. Barker's excellent treatise on the nervous system published at the beginning of this year, brings the history of the neuron controversy up to date.

It should be remembered, however, that the "Neuron Hypothesis," "Neuron Theory," or "Neuron Concept" is not, properly speaking, a theory at all. It explains nothing. It is a statement, supposed to be true, that every nerve-cell, with all the parts that belong thereto (axon, collaterals, terminal arborisations, dendrites) is anatomically distinct from every other nerve-cell. The conclusions with regard to physiological autonomy and the restriction of pathological processes which are often regarded as deductions from the "Neuron Theory," are really deductions from the Cell Theory of Schwann, and would equally hold good if all the neurons of the body were continuous one with another. When Hooke, in 1696, examining a slice of bottle cork, observed that it is divided into chambers like the "cells" of honeycomb, he supposed that the partition walls of these chambers were impervious. When, in 1839, Schwann applied the "cell theory" to animals, he imagined all plants and animals to be colonies of separate and distinct "cells." The discovery by Sachs, Gardiner and Russow that a plant is not, as Schwann supposed it to be, a colony of separate cells, but a single protoplasmic unit imperfectly divided into cells by perforate cellulose septa, does not in any degree invalidate the cell theory. The discovery that the substance of any given cell is united by myriads of protoplasmic threads with the substance of the cells by which it is surrounded does not affect our conviction, based on innumerable observations, that every cell grows, lives and dies as an individual. The trophic individuality of the nerve-cell or "neuron" is a matter of observation. We have no reason to think that if every neuron were continuous with other neurons at a multitude of points the trophic control of one neuron would extend to any parts of its neighbours. Nerve-cells are uninuclear. Each nucleus is therefore the capital of a cell territory. Whether or not the economic processes carried out within the territory are in any way controlled from the capital, it is quite certain that each territory is self-governing. It may be easier to grasp, in the case of discrete cells, the fact that the metabolism of the territory stops at its boundary, than it is to realise that it stops at the histogenetic boundary of confluent cells; but we are acquainted with many tissues in which the cells are in various ways and in varying degrees united together, yet in none of these is there reason to think that confluence of structure indicates co-operation in nutritive processes. Each individual cell grows, carries on the business of its life, and dies, as a unit.

The belief that the neurons are discrete is based upon the appearances presented by chrome-silver and methylene-blue preparations. As to the distinctness of the coloured elements there can, as a rule, be no manner of doubt; but even here the rule is not absolute. I have found instances of the union by coarse bridges of two or even three cells in all classes of nerve-cells. Dogiel, Masius and others also maintain that, in certain cases, the dendrites anastomose. But such a union of homologous elements is of little interest. It merely points to their origin by cell-division. The neuron-statement is based upon the supposition that heterologous elements are never directly united together. Chrome-silver and methylene-blue preparations appear to demonstrate the structural isolation of heterologous elements. Histologists have accepted their evidence as conclusive on this point. In a series of papers published since 1885, and especially in my presidential address to the Neurological Society of London, in 1896,[1] I have urged that the credibility of these witnesses should be further tested before their evidence is accepted as conclusive. At one time neurologists held, universally it may be said, a contrary opinion. Since the publication of Apáthy's paper in 1897 it has been recognised that, for invertebrates at any rate, the neuron-statement is untrue.

The union of homologous elements by means of their dendrites not being to the point, there are only two ways in which neurons can be mutually connected. (1) The axon of a central cell A may divide to pass without arborisation into several smaller (distributive) cells B ; or, in other words, the apparent axons of several small cells B may be the subdivisions of the axon of a larger cell A ; (2) The terminal arborisations of the axon of A may be continued into the dendrites of B. I shall endeavour to prove that unions of both kinds occur.

In recent years histologists have shown an ever increasing tendency to lay stress upon the direct connection of basket-like arborisations with the bodies of nerve-cells. Some histologists appear, indeed, to look upon the various forms of "basket," "pericellular network," and "pericellular tangle" as the chief means by which neurons are linked together. The subject is one of the greatest difficulty. But it appears to me on general grounds highly improbable that the basket is the most important terminal apparatus through which one neuron influences another. Phylogenetically it cannot be so: for it is through the neuropil that the branchings of associated neurons are first connected. Again, it is not a universal method of association, since no baskets are described as surrounding some of the most important cells, those of the spinal cord, for example. Looking at the matter from the opposite point of view the widely branching dendrites of such cells as the pyramids of the cortex or cells of Purkinje must have a significance, as collecting apparatus, which far surpasses that of any system of direct cell-body endings. The growth of a Purkinje cell is most instructive in this respect. When it is first recognisable as a distinct element (fig. 27) it is an oval cell from which an axon is already beginning to grow out. Soon its cell-body seems, if the chrome-silver method is to be trusted, to receive afferent filaments (fig. 28); at any rate it is always shaggy at this stage. Then with great rapidity its copious branching system of dendrites extends towards the surface—coarse and woolly as if connected with multitudes of fibrils—while the cell-body becomes clean and free from filaments (fig. 29). It seems to me incredible that any direct ending of nerve-branches in or around the body of a Purkinje cell, if there be such endings, can compare in importance, as a mechanism of association, with the elaborate dendrites of the cell.

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[1] Hill. "The Chrome-silver Method," BRAIN, 1896, p. 1.

Amongst descriptions of arborisation-endings within cells those of Held[1] are the most precise. Using iron hæmatoxylin staining Held exhibits certain minute rod-like particles or "neurosomes," which are closely aggregated in the axon and its terminal ramifications, and more widely scattered in the neuroplasm of the cell-bodies. By their aid he is able, as he believes, to follow the nerve-terminals given off by the fibre-baskets, which surround the cells of the nucleus trapezoides and other nuclei, into the substance of the cells and their dendrites. He shows these filaments entering the cell-bodies and penetrating even as far as their nuclei. But he believes that, having entered the cell-body, these filaments end abruptly, and do not pass out of it through its axis-cylinder. Held is therefore an upholder of the neuron theory, *i.e.*, of the theory of the discontinuity of the neurons, with this modification: that the end-branches of one neuron may actually penetrate into the body substance of others.

Had Held used a precipitable stain only, we should have discounted his results by the considerations—(1) that his fixing agents—alcohol, chloroform, acetic acid, and picro-sulphuric acid—cause the formation of coagulation products, which may have no existence in life, and yet be coloured after death—this is an objection to which Held himself calls attention; and (2) that iron hæmatoxylin gives a solid deposit in the cell substance. There is no problem in minute anatomy more puzzling than that of the weight to be assigned to precipitates within tissue elements as indicative of structural differentiation. For example: I have endeavoured to check Held's results by using Weigert's hæmatoxylin method after carmine-alum, and then over-bleaching the sections in ferrid-cyanide of potassium. Cells so treated are seen to be full of black granules; but the granules are not rod-shaped like the "neurosomes," nor can I detect any indications of a differential arrangement. Indeed, the size of the granules, which are always round or oval, and their condition of aggregation appear to depend upon the exact treatment to which they have been exposed.

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[1] Held. "Beiträge zur Structur der Nervenzellen und ihrer Fortsätze," *Arch. f. Anat. u. Physiol.*, Anat. Abth., 1897, p. 204.

Held's results have not been left unchallenged, as may be seen in a paper by Veratti,[1] which is illustrated with very striking figures of the author's own results. Turner and Hunter[2] also, using methylene blue, *intra vitam*, conclude that the filaments of the pericellular network do not enter the cell-bodies but lie upon them, and are continued on to their protoplasmic processes. The whole subject is one upon which it is permissible at present to retain an open mind. Especially is it legitimate to consider that the nature of these pericellular baskets is not yet definitely settled, when one reflects that neither Held's method nor the methylene blue exhibit the conducting fibrils of the nerves, but only the neuroplasm in which they lie. For my own part, I am inclined to believe that Turner and Hunter are right in supposing the fine nerve-filaments to lie upon the body substance of the cells which they invest. It appears to me that when nerve-fibres are split into their constituent fibrils, or fine bunches of fibrils, the nutrition and insulation of these fine fibrils, which doubtless consist of conducting elements invested in neuroplasm. is in some way provided for by bringing them into juxtaposition with the cells near which they are passing, and the large dendrites of these cells. The neuroplasm of these cells is in some way favourable to the vitality of the fine fibres. It provides for the insulation and nutrition of the fibrils throughout the distance through which they lie upon it. To this subject I shall recur when speaking of granules.

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[1] Veratti. *Sul alcuni particolarità di struttura dei centri acustici nei mammiferi*, Pavia, 1900, pp. 81, 7 plates.

[2] Turner and Hunter. "On a Form of Nerve Termination in the Central Nervous System demonstrated by Methylene Blue," BRAIN, 1899, p. 123.

With these preliminary observations I pass to the consideration of the question which I propose to discuss in this paper, namely: *Are the neurons genetically and structurally discrete; or do the distributing processes of one neuron form true anastomoses with the collecting processes of other neurons?*

As evidence of union of neurons I propose to consider:

(1) The relation of the terminal arborisation of axons to so-called "granules."

(2) The neurons of the sympathetic system.

(3) The evidence that "thorns" are portions of conducting fibrils surrounded by the neuroplasm of the collecting processes of nerve-cells.

(1) GRANULES.

When the chrome-silver method first came into use the extraordinarily distinct pictures of large nerve-cells which it presented in the cortex cerebri et cerebelli, the spinal cord, the olfactory bulb and elsewhere, attracted universal attention. They were so sharply defined and apparently so complete that they distracted attention from the other elements of which nerve-tissue is composed. Even now we frequently meet with an attempted counting of the "nerve-cells" in the cortex or in the central nervous system as a whole, in which no account is taken of the granules and other small cells! Yet the granules are far more numerous than the pyramids or cells of Purkinje, and each granule is equally complete, and equally entitled to the designation of "nerve-cell" or "neuron." When Pedro Ramón showed the axons of the granules of the cerebellum, and his brother, S. Ramón y Cajal, the axons of the granules of the retina, they demonstrated that each of these granules is a perfect nerve-cell, with dendrites and axon and all other features of a neuron. They differ from the great cells which give off efferent fibres in no respects other than size. I have shown that the granules of the olfactory bulb (which other histologists set aside as "amacrine" cells or even as gleial cells), have axis-cylinder processes and thorny protoplasmic processes, and are therefore also complete nerve-cells;[1] a fact of some importance, apart from its particular application, because it leaves it open to us to conclude that when, in the future, we see a cell which has all the ordinary characters of a nerve-cell, and especially when it bears branching *thorny* dendrites it cannot be a gleial cell, however difficult we may find it to demonstrate the axis-cylinder. As further evidence of the nervous nature of the granules of the olfactory bulb Blanes[2] has pointed out that they readily take the vital methylene-blue stain, whereas the gleial elements remain uncoloured; and further that they are to be found with their characteristic form in vertebrates which do not possess in this situation any typical gleial cells. It is clear that no plan of the structure of nerve-tissue is complete which does not include the granules, or which, in any situation in which they occur, sets them aside as non-nervous elements. Indeed they are just as important elements or units as the largest nerve-cells.

When a nerve-fibre reaches a muscle-fibre, or the modified muscle-fibre of an electric organ, its terminal arborisation, or the sarcogleia in which it is embedded, contains nuclei. In the end-plates of the frog these nuclei, which rest immediately upon the nerve-twigs, were termed by Henle the "nuclei of the branches of the axis-cylinder," and distinguished by him from the nuclei of the sheath of epilemma. No one, I think, will deny that there are, in the end-plate, nuclei which are different in appearance to those of the muscle substance. There are two, if not three, forms of nucleus on the fine nerve-twigs, which are distributed to the electric organ of the skate; but I do not find it possible, after allowing for the nuclei of the sheaths of the nerves (after they have lost their myelin), to distinguish with certainty any nuclei which clearly belong to the nerve-twigs. It seems to me quite possible, however, that Henle's nuclei of the branches of the axis-cylinder are nuclei of nervous elements through which the conducting fibrils of motor nerves are distributed to muscle-substance. If this conjecture be justifiable the conception of a motor neuron is incomplete unless the minute cells (daughter cells of the large cell in the anterior horn of the spinal cord?) are included in the neuron. This is equivalent to saying that the theory of the individuality of the neuron breaks down. I lay no stress upon this hypothesis of the mode of ending of motor nerves, however, but use it merely as an illustration of the mode of ending of ascending (sensory) fibres which I am about to describe.

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[1] Hill. "Notes on Granules," BRAIN, 1897, p. 125. It was only after making thousands of preparations that I was able to demonstrate the axis-cylinders; and so curiously capricious is the chrome-silver colouration in this matter that, although I am always glad to show the sections in which axons are visible, I am afraid to part with them, since I have but two or three!

[2] Blanes. "Sobre Algunos puntos dudosos de la estructura del bulbo olfatorio," *Riv. trimestr. microgr.* 3, 1898.

The crucial test of the neuron theory lies, as it seems to me, in the proof that fibres which ascend from cells in the cerebro-spinal axis end freely in the cortical fields. If the ascending fibres pass without breach of continuity from cells in the spinal ganglia or in the nuclei of Goll and Burdach into cells in the cortical field—if, that is to say, they start in one large cell (or, accepting Apáthy's findings, if they originate with a "fibre-cell," pass through a "ganglion-cell") and join several small cells—the neuron theory falls to the ground. It is true that various qualifications are introduced by recent writers into the expression of the theory; "relative individuality of the neurons" is often substituted for the definite expression of absolute independence; but if as a mechanism each nerve-cell with its collecting and distributing processes is not an anatomical integer but a part of a chain of cells, the theory loses all significance.

It is generally assumed, in the case of the cortex cerebelli at any rate, that afferent fibres come into relation with "granules" and that the axons of the granules transmit the impulses, which the afferent fibres bring, to the more superficial elements of the cortex. Ramón y Cajal represents the branching afferent fibres (mossy fibres) as being in relation with the clawed dendrites of the granules, and the bifurcating axons of the granules as in relation with the dendrites of the Purkinje cells. Neglecting all other elements and reducing the scheme of connections to a diagram, the conducting arc of the cortex cerebelli consists of a mossy fibre—its end-branches, granules; their axons, dendrites of a Purkinje cell—its axon. The granules are, according to this scheme, secondary or tertiary neurons of the chain leading from sensory cells to the cortex cerebelli, and each granule is supposed to be as independent, as self-contained, as the larger neurons between which they are intermediaries.

In my preparations I find a few instances of granules which (figs. 1, 2 and 3) are distinctly connected with fibres of the arbor vitæ on the one side and with divaricating axons, passing between the cells of Purkinje to the molecular layer, on the other side. I find a very large number of granules which are connected with fibres from the arbor vitæ. In some cases the axon of the granule passes with a much twisted course towards the arbor vitæ (figs. 4, 5). In the two specimens figured (4, 5) the connection of the granule and the nerve-fibre occurs at a point which will afterwards become the clawed end of one of the arms of the granule.[1] Fig. 6 shows a granule the axon of which joins, apparently, a branch of a fibre from the arbor vitæ which ends by ramifying in the molecular layer. Figs. 7 and 8 illustrate a not uncommon disposition of the axon of a granule in which, before it reaches the sheet of Purkinje cells it bifurcates, giving one branch to the molecular layer and another which runs inwards towards the arbor vitæ. In fig. 9 is seen a granule the axon of which has an extraordinarily tortuous course and gives off several branches in the granular layer as well as one or more branches to the molecular layer.

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[1] It will be understood by everyone who has worked with the chrome-silver method that when I assert that a fibre is continuous, or that two fibres are in connection, I wish to imply that all attempts to prove discontinuity by careful focussing, by oblique illumination, &c., have failed. When two opaque black objects are superposed or in close juxtaposition, they appear to be in continuity. It is never possible to make sure that this is the case.

It will be noticed that none of the granules figured have the ordinary form of the cerebellar granule. This, as is well known, is a round cell with four or five dendrites ending in clawed hands and a single axon which divaricates into two long fibres in the molecular layer. But granules of this form do not make their appearance until comparatively late in development; in puppies at about 18 days, kittens at about 14 days, hedgehogs at about 18 days. It is, I fear, impossible to give exact dates owing (1) to the unreliability of the chrome-silver method, and (2) to the fact that the histogenetic development of the cortex cerebelli takes place gradually. Granules having the immature, carrot-like form represented in figs. 1 to 8 are to be found long after the first mature granules have made their appearance. To make this part of the subject clear it will be necessary to give some account of—

The Development of Ordinary Granules.

In a paper published in 1889 Bellonci and Stefani[1] gave an accurate account of the changes in the external nuclear layer, which might have suggested the migration of the granules subsequently discovered by Rámon y Cajal. They described the formation of a molecular layer containing some scattered cells before the overgrowth occurs, from behind forwards, of the nuclei of the ependymal stria of the velum medullare posterius. As the nuclei spread forwards from this stria (the Rautenlippe of His?) their mitotic figures indicate active division. For some time before the appearance of the cells of Purkinje, and still more after these are differentiated, the nuclei are distinguishable into two zones—an external, in which the nuclei are round and rich in caryokinetic figures; and an internal, in which the nuclei are elongated transversely and rarely show caryokinetic figures. The molecular substance is chiefly made up of transverse fibrils which Bellonci and Stefani presume to be derived from the elongated cells. "The deepest nuclei of this layer appear uncoloured and are consequently seen with difficulty. As the molecular layer grows in thickness they are destroyed in great numbers." Löwe[1] had previously described the molecular substance as formed by the fusion into a mass of the cell bodies of these nuclei, the nuclei becoming vesicular and gradually disappearing.

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[1] Bellonci et Stefani. "Contribution à l'histogénèse de l'écorce cérébellaire," *Arch. ital. de Biologie*, xi., 21.

In the light of Rámon y Cajal's observations, to which reference will be made immediately, it is clear that the disappearance of the nuclei is due, not to their degeneration, but to their migration past the cells of Purkinje into the granular layer.

Simultaneously with Bellonci and Stefani, Lahousse[2] described in very similar terms the appearance and overgrowth of the external nuclei. He named this layer "the layer of Obersteiner," since the Viennese professor was the first to describe it;[3] but he prefers to call the cells of which it is composed "cellules conquérantes" or "cellules de renfort." "The reinforcing cells multiply abundantly and invade, from behind forwards and from within outwards, almost the totality of the external surface of the cerebellum, with the exception of the median line and the posterior part of the inferior vermis, in the neighbourhood of the median line."

It is evident from the descriptions just quoted that the cells of the external granular layer have a secondary origin. They are not formed from the general mantle-layer of the cerebellum. It is curious and probably significant that their site of origin should correspond nearly with that of the spinal ganglia, and that each little cell should be in the mode of its growth—a fusiform cell converted into a round cell with an axis-cylinder in the form of a T—a root-ganglion cell in miniature, *plus* five or six clawed arms. We owe to a very remarkable piece of histological work carried out by Rámon y Cajal the proof that the granules undergo the transformation just described.

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[1] Löwe. *Anat. u. Entwicklungsgeschichte d. Nervensystems*, vol. ii., Leipsic, 1883.

[2] Lahousse. "Recherches sur l'ontogénèse du Cervelet," *Arch. de Biologie*, viii. (1888), p. 43.

[3] Obersteiner. "Beiträge z. K. von feineren Bau der Kleinhirnrinde," *Sitz. d. K. Akad. d. Wissensch*, Vienna, 1860, and again in *Biologisches Centralblatt*, iii. (1883).

According to Ramón y Cajal, the precursors of the granules are fusiform cells, tapering into a fibre at each end (figs. 18 and 19).

That Ramón y Cajal's description of the transformation of fusiform cells into granules is right is borne out by appearances such as are shown in figs. 18, 20, and 22, as well as by the fact that the fusiform cells are not to be found in adult cerebella. There are, however, some difficulties in explaining how the one kind of cell is transformed into the other.

It is, for example, to be noticed that in the embryonic state of these granules—when they are fusiform or "fibre-cells"—there is an obvious distinction between the thread-like axon on the one side and the thicker process on the other side, which has the appearance of a dendrite (fig. 18), and yet both alike, according to Ramón y Cajal, become horizontal limbs of the T-shaped axon of the granule. Further, certain noteworthy physiological difficulties result from this. In the first place, since the granules cannot be supposed to have any function until they have, by sinking beneath the layer of Purkinje cells, established connections with afferent (mossy) fibres, it is remarkable that their processes should be so long. The length of the tangential fibres, to which the fusiform cells which Ramón y Cajal regards as embryo granules give rise, is very remarkable. I have traced them in a puppy for fully 1½ mm. A study of the histogeny of the nervous system leads to the conclusion that the growth of conducting strands, if it cannot be described as a response to function, keeps but little, if at all, ahead of function. Yet here we have what, to all appearance, are well-developed nerve-cells and fibres which cannot, so far as we can understand the conditions which obtain in the embryonic cerebellum, take on functional activity for some time. We should have expected to see the lateral extension of the limbs of the T delayed until there was a possibility of impulses passing into them up the vertical limb. In the second place, if the view universally held as to the function of the granules—that they collect impulses from the afferent (mossy) fibres and distribute them to the dendrites of the Purkinje cells by means of their divaricating axons, a view enunciated by Ramón-y Cajal in his Croonian lecture—be correct, the distinction between cellulipetal and cellulifugal conduction, in the case of granules, breaks down. Both the axon and the dendrite of the precursor of the granule conduct (when they become the two limbs of the T-formed axon) outward from the cell. It may be said that a similar difficulty has to be met in the case of the cells of spinal ganglia; but the cases are not quite parallel. It is open to us to consider the distal process of a root-ganglion cell as the dendrite, the proximal process as its axon; since the one conducts cellulipetally, the other cellulifugally. Of course, if Apáthy's theory of "nerve-cells" and "ganglion-cells" be substantiated, this point loses its significance, since the root-ganglion cells must be "nerve-cells," from which fibrils are developed, which grow both outwards to the sensory cells and inwards into the axial cells. If the description given by Ramón y Cajal of the formation of the granule be correct, the cell-body withdraws from the fibre, just as in the case of a root-ganglion cell; but the horizontal limb of the T is not a direct conductor from left to right, but a distributor of impulses to the left and to the right.

Here I ought to mention a difficulty which has met me in tracing the origin of granules from these fusiform cells. In long hardened tissue I find these fusiform cells—which might be termed "fibre-cells"—in the developing molecular layer in very great numbers; but I have never succeeded in demonstrating the first step in their conversion into granules. I find granules with a carrot-like apical process which points towards the granular layer, and a very short T-process which branches right and left in fine nerves (fig. 20), which looks as if it might have been derived from a fibre-cell; but after a most prolonged search, I have failed to see the first step in the pinching together of the two processes of a fibre-cell. Again, in certain animals, especially the puppy (fig. 18), the fibre-cells appear to be larger and better developed than the first-formed granules. Lastly, these well-developed fibre-cells often show fine branches given off vertically to their lateral continuations, both axonal and dendritic (fig. 19). Such branches appear to have no place in the constitution of the granules.

Athias[1] insists that the bipolar cells are at first connected with the surface by a thick vertical process. Ramón y Cajal figures the same condition. But as soon as the body of the granule has withdrawn from the horizontal fibre it shows a thick process directed towards the granule layer. This reversal is certainly very remarkable, and I have looked carefully for transitional stages, but without success.

Occasionally I find a developing granule with a thick apical process which points towards the surface; but this condition is rare, and I think that Cajal, Popoff, Athias, and others, have confused with developing granules cells of a different kind (figs. 15, 16, 17) which are to be found in the deeper part of Obersteiner's layer, or just below it. Under any circumstances it is very difficult to understand the transitions through which a truly bipolar cell (fig. 18) passes in becoming a granule. At first it has an axon to one side and an apical process to the other. Then, according to the received account, it has an apical process directed towards the surface, and axons to right and left. Next it has a centrally-directed apical process and axons right and left. It appears to me that three different kinds of cell are developed in the molecular layer or superficial to it—A and B, the granules which I have called carrot-granules, and the ordinary granules from Obersteiner's layer—C, the cells of Cajal, either from the deepest part of Obersteiner's layer or from the underlying superficial part of the mantle-layer.

Our information with regard to the histogenesis of the cerebellum is far from complete, but the following points seem to stand out clearly: (1) The nuclei found at birth and for some time subsequently, outside the sheet of cells of Purkinje in the cortex cerebelli, are much more numerous than the nuclei of the molecular layer in the adult. (2) There is no sufficient indication of cell division on the ventricular side of the cells of Purkinje to account for the formation of the granular layer. Hence the granules are migrants from the superficial tissue. (3) From Obersteiner's layer are developed granules, "carrot-granules," Cajal's cells, and the small cortical cells or stellate cells of the molecular layer. (4) In the mantle proper are developed gleial cells, Golgi cells, and Purkinje cells.

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[1] Athias. "Recherches sur l'histogénèse de l'écorce du cervelet." *J. de l'Anat. et de Physiol.*, XXXIII. (1897), p. 372.

The further stages in the growth of the granules have not been described, but they are of great interest. As soon as the granule has passed through the layer of Purkinje cells its apical carrot-shaped process increases considerably in length and gives off several slender side branches (figs. 1, 3, 23) which divide two or three times into long slender twigs. In this stage it shows none of the clawed arms which are so characteristic of the fully formed granule. These appear later as lateral branches, very short at first (fig. 25). In the meantime the long apical process makes its way towards the arbor vitæ, which it frequently enters, becoming lost among the fibres (fig. 1). Its appearance at this stage is strongly suggestive of its feeling down amongst the fibres for nerve connections.

In puppies until they are about 18 days old, hedgehogs 18 days, kittens 2 weeks, none of the typical round granules with four or five arms ending in claws are to be found. All the granules have the appearance shown in figs. 1, 2, 3, &c. It is at this stage that the granules show a double connection—with the fibres of the arbor vitæ on the one side, and with an axon divaricating in the molecular layer on the other.

It is also to be noticed that the granules, which at first are placed with their long axes horizontal (fibre-cells), are next placed vertically, as they migrate past the cells of Purkinje, and lastly, more or less horizontally again as they approach the arbor vitæ.

The meaning of the "claw" is at present obscure. The claw assumes, in chrome-silver preparations, many different forms. Sometimes it appears as a hand with four or five fingers. Occasionally it is a complete basket, which is often larger than the granule which it appears to enclose; too large, that is to say, to be in contact with the body substance of the granule which it envelops. Every intermediate condition between these two forms is seen. Every now and again one sees a basket which appears to re-form into a fibre, as if the arm of the granule which had divided into a basketwork were in continuity through this basketwork with a (? mossy) fibre.

In my paper on the Chrome-silver Method I called attention to the fact that the baskets of Ramón y Cajal which invest the cells of Purkinje are frequently seen to reunite beneath the cells into bunches of fibres, which enter the granular layer. In other words, the tassel of fibrils depends beyond the base of the Purkinje cell. Instead of the tassel of fibres being closely applied to the surface of a Purkinje cell it is loose and large, and its twigs surround the axon of the cell. This observation is confirmed by Dr. John Turner, staining with methylene blue.[1] On the other hand, fibres which branch in the granular layer break up into baskets which approach the cell from below. Fibres are frequently seen in the granular layer which have just the same relation to the Purkinje cells as the branches from the axons of Cajal's cells, except that whereas the latter approach them from below, the former approach them from above. It is quite possible that the two kinds of basket are continuous, or, to speak more correctly, that there is only one kind of basket into which the fibre from the one side breaks up, and from which the fibre on the other side is re-formed; the chrome-silver method revealing sometimes the one half of the basket, and at other times the other. It is very difficult to account for such an arrangement as a basket-work which envelops the body of a cell without establishing any connections with it; and I hesitate to suggest a hypothesis, but it seems to me not impossible that where connection is to be established between two kinds of nerve-fibres the fibres break up into their constituent fibrils, which rest upon the body of a neutral cell. If this be possible, the cell of Purkinje in some way provides for the insulation and nutrition of the isolated fibrils. In the same way the baskets into which the arms of the granules appear to end may be bunches of elementary fibrils separated out at the spot where the arm of a granule joins some other kind of fibre. I shall amplify this hypothesis later on.

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[1] Turner. "A Note on the Staining of Brain in a Mixture of Methylene Blue and Peroxide of Hydrogen." BRAIN, 1900, p. 524.

Carrot-Granules with Centripetal Axis-Cylinders.

In 1896[1] I described and figured granules whose axis-cylinder processes join the fibres of the arbor vitæ. They are distinguished by their carrot-like form, and are only found in tissue which has been hardened in bichromate (with or without osmic acid or formalin) for a long time.[2] Subsequently (BRAIN, 1897, pp. 125 and 466) I described and photographed granules of extremely similar form, which I had found in the molecular layer. After Ramón y Cajal's description of the origin of the granules from bipolar cells, I am satisfied that those which I described are embryonic granules, strangely unlike to adult granules though they are. Carrot-granules with centripetal axis-cylinders are, however, cells which cannot be confused with developing clawed granules. They are most numerous at the apices of the folia, when they appear (as shown in fig. 13) as cells of considerable length. They always take a brown colouration, the nucleus remaining clear. Their apical processes divide two or three times as they extend outwards towards the cells of Purkinje. Their axis-cylinders may be undivided, or they may give off branches which return towards the surface. In the developing cortex cerebelli, at an early stage, cells are to be seen which cannot be embryonic granules of the ordinary form (figs. 15, 16, and 17). They are placed vertically to the surface. Their apical processes reach at first to the pia mater, where they usually end in a knob, which rests against this membrane. Their axons take a centripetal course. Subsequently the apical process withdraws from the pia mater, and the cells sink more deeply in the molecular layer. Their axons frequently give slender lateral branches. It is possible that these cells will grow into Golgi cells or even into cells of Purkinje; but considering the very early date at which cells of both these classes assume a well-developed appearance, I am disposed to think that the fusiform cells just described are not destined to undergo this transformation, but are developing carrot-granules. The cells represented in fig. 17 in the molecular layer certainly appear to be the same as those which are represented in fig. 13 in the granular layer.

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[1] BRAIN, 1896, p. 35, fig. 14.

[2] *Method.*—All the sections figured in this paper were prepared from tissue which had been immersed in bichromate of potassium and osmic acid or formalin for a long time. When endeavouring to ascertain the nature of the chrome-silver reaction I varied the length of time during which the tissue was immersed in the respective fluids within very wide limits. This research was undertaken without any thought of discovering new elements of nerve-tissue, but merely with a view to ascertaining the nature and the limitations of the method. Unlike Lenhossék, Ramón y Cajal, and others, I find that nothing is lost by a long immersion in the chromate. I know of no structural feature which is exhibited in tissue hardened in bichromate of potassium and osmic acid for a few days, which is not also to be found in tissue which has been hardened in this mixture for two or three years before being transferred to silver nitrate. On the other hand, I have never found "carrot-granules" or the most delicately-branched fibres of the granular layer in tissue which has not been hardened for at least a month; and I am disposed to think that they are best seen in tissue which has been hardened for at least three months.

After a year the tissue becomes very brittle and difficult to handle, and since nothing more is to be gained by such a prolonged hardening, I regard the best length of time for immersion in the chromate as from three to six months. This method is especially successful with young animals—cats, dogs, &c., of not more than a month old. Among my specimens from adult brains which have lain in bichromate of potassium and osmic acid for more than a year the greater number are complete failures. Some, on the other hand, are admirably coloured. Evidently, therefore, other conditions beside the long hardening help to determine the success or failure of the impregnation. How admirably it may succeed is well shown in fig. 12, of a Golgi cell from the cerebellum of a cat twenty-seven days old, hardened for five months. This cell lies at the apex of a convolution, and it is curious to note that its branched axis-cylinder is continued by a very delicate fibre to the extreme base of the convolution, a distance of at least 2 mm. Whether or not this revelation is due to the method it is impossible to say, but I have never seen such a connection in a specimen hardened as directed by Golgi or by Ramón y Cajal. Nor is it in accordance with any description of these cells of Golgi's type II., the specific character of which is supposed to lie in the complete arborisation of their axons within the cortex.

It is to be noticed that the dendrites of the Golgi cells are destitute of thorns. In this respect they contrast in a very marked way with the extremely thorny dendrites of the Purkinje cells, fragments of which are to be seen on the right and left of the figure.

I have found carrot-granules in very large numbers in rats (up to 12 days), kittens (to 14 days), puppies (to 21 days), hedgehogs (to about 18 days). I have never found them, with certainty, in adult cerebella. It is true that I have found a few doubtful specimens in adult sheep, but they were not sufficiently distinct for me to lay any stress upon them as proving that the granule with centripetal axis-cylinder is a permanent structure. On the other hand it should be noted that these granules make their appearance only after long hardening, and I have but very little adult tissue which has been so treated. One is afraid to lay down any rule for the chrome-silver reaction, the next set of sections prepared may prove it fallacious; but in several specimens of tissue which were tested by the nitrate of silver at intervals during the hardening process, the granules with centripetal axons were not found until after long hardening, the earliest case being after immersion for five months in bichromate and osmic acid.

Are the carrot-granules with centripetal axons, like the carrot-granules with centrifugal axons, embryonic cells? A very large number of observations have failed to reveal any transitional forms, and it is difficult to conceive, if they be embryonic, into what adult elements they grow. It might be supposed that they grow into Golgi cells; but the Golgi cells are remarkably mature in appearance in sections which abound in carrot-granules; indeed, they are amongst the earliest of the cerebellar elements to take on an adult form. Again, the Golgi cells are always supposed to belong to "Golgi's type II.," that is to say they are cells with short axis-cylinders. (A curious instance of an axis-cylinder which does not terminate by arborisation in the vicinity of the cell is shown in fig. 13; but this does not justify us in drawing the conclusion that all Golgi cells have connections with the fibres of the arbor vitæ.) I cannot at the present time see any indication that the carrot-granules are young Golgi cells. The only alternative left open is, therefore, that either they are cells found in the young animal which disappear in the adult, or that they are cells which the chrome-silver method reveals in the young animal (owing to its peculiar suitability for embryonic tissue) and does not reveal in the adult.

If these cells belong to a distinct and hitherto unrecognised class it is most important that they should receive a distinctive name. The application to tissue elements of the names of their discoverers is to be deprecated except in very special cases. That Purkinje, Golgi and Cajal should have written their names on the cerebellum is no more than their due, but even in their case the application of the name should be rigidly limited. The cells most intimately associated with Cajal are the basket cells. Cells of the molecular layer which do not form baskets must bear another name, and probably none is better than "small cortical cells," proposed by Schäfer. Golgi's cells are the remarkable large cells with branching axis-cylinders. Some of them lie amongst the cells of Purkinje and branch in the molecular layer, whereas others are restricted to the granular layer. The application of Golgi's name to other cells, and especially to the granules, is extremely confusing. Probably the time-honoured name "granule" is the least likely to be misunderstood. If the cells which I have described are distinct from the typical round granule, the term "carrot-granule" will probably as well as any other mark this distinction and at the same time convey to the reader's mind the idea that they are so small as to belong to quite a different class of element from the Golgi-cells. Their rarely-branching axis-cylinder continued into the arbor vitæ completely separates them from the "cells with short axis-cylinder of Golgi's type II."

Since the cells of Purkinje are the only recognised cells with descending axons, I have spoken of the carrot-granules as connected with ascending fibres; but this is, of course, a hypothesis in support of which we have not, at present, any evidence.

(2) SYMPATHETIC SYSTEM.

When evidence derived from the central nervous system led to the formulation of the neuron theory, it was concluded that the cells of the sporadic ganglia must be brought into line with the neurons of the axis. Instead of the sympathetic cells being "distributive," in the sense that each receives one nerve-fibre of a certain thickness and gives origin to a number of thinner fibres—the afferent fibre being usually medullated and the efferent fibre non-medullated—it was assumed that the thicker fibre is the axon, the thinner fibres dendrites. But the histological evidence upon which this view is based is not by any means satisfactory. I may summarise my doubts as to its justice under the following heads :—

(*a*) The alleged dendrites do not present the characters by which dendrites are usually distinguished. This is shown in all figures with which I am acquainted (see, for example, Köllicker's "Gewebelehre," vol. ii., figs. 834, 835), and therefore I have not thought it necessary to prepare fresh illustrations. The end branches of the so-called dendrites are exceedingly slender filaments, often of a great length. They are usually varicose—a very characteristic feature of the finest nerve-fibres and a rare feature in dendrites. They are destitute of thorns. For reasons which will appear later I regard thorns as the distinctive markings of true dendrites, but on this point I possibly take too strong a position.

(*b*) The so-called dendrites may often be followed beyond the limits of the ganglion. Where stained cells lie near the point of exit of a gray ramus the so-called dendrites frequently pass as a bundle of very slender fibres into the ramus.

(*c*) If it be accepted that the branching processes are dendrites it is very difficult to assign to them any function. Setting aside the doctrine of their purely nutritive function, dendrites are regarded as establishing connections between the cells to which they belong and the end-branches of axons of cells lower or higher in the system. The tissue of which the ganglia are composed is however peculiarly unfavourable for such connections. It is a dense connective tissue packed with large nerve-cells and traversed by innumerable nerve-fibres. There is no "gray matter." There is none of the tissue which, in the cerebro-spinal axis or in the ganglia of invertebrates, seems to be essential for the establishment of such connections.

(*d*) Failing communications between end-branches and dendrites, the manner in which the neurons of the axis influence the neurons of the ganglia is insufficiently explained. It appears to be limited to the various forms of "basket" which have been described. Ramón y Cajal, Retzius, Kölliker and others, have described certain of the "dendritic branches" as forming baskets, upon which Kölliker very properly remarks: "Welchem Verhalten ich jedoch bei genauer Ueberlegung keinerlei physiologische Bedeutung zuschreiben kann und dasselbe nur für etwas zufälliges erklären muss" (*loc. cit.*, p. 853). The whole question of baskets, pericellular plexuses, and pericellular tangles is most obscure. Their primary purpose does not seem to me to be to establish a connection between end-branches and the cell-body which they invest; to this question I have already referred, suggesting a hypothesis, when treating of the granules of the cerebellum.

(*e*) It is beyond question that the præganglionic nerves (white rami, &c.) contain fewer fibres, and these larger (medullated) than the postganglionic nerve. As Gaskell's[1] careful analysis of the sympathetic system showed, the ganglia may be looked upon as stations in which medullated fibres are replaced by bundles of non-medullated fibres. If the old view that the cells of the sympathetic ganglia receive each a large fibre and give off a number of fine fibres be discarded, the enormous multiplication of fibres which occurs in the ganglia must be effected by the subdivision of the axons of their cells Such a subdivision is assumed; but in cases in which that process of a cell which is, beyond doubt, its axon can be followed for some distance, it is, so far as my own observations go, conspicuous for the absence of collaterals or side branches of any kind.

(*f*) If the neuron theory be applicable to the sympathetic system, which is, so far as we know, entirely an efferent system, the præganglionic fibres must end by arborisation, the axons of the cells must constitute postganglionic fibres. I have made various preparations with a view to ascertaining if this is the case. Owing to technical difficulties these preparations are not quite satisfactory, but they leave me in little doubt but that the axons of the cells of the sympathetic ganglia are directed towards the præganglionic fibres, *i.e.*, towards the cerebro-spinal axis. In the superior cervical ganglion, for example, the axons leave the ganglion at its cervical end. This is a question upon which I hope to give a further report in a short time.

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[1] Gaskell. "Nerves which Innervate the Visceral and Vascular Systems." *Journal of Physiology*, vii., 1.

(*g*) The mode of origin of the sympathetic ganglia is suggestive of a permanent connection between their cells and cells in the cerebro-spinal axis. The sympathetic neuroblasts are cells which at a very early stage have migrated from the neuro-epithelium which forms the cerebro-spinal axis and the spinal ganglia. It may well be that they retain, during their migration outwards, a connection with the cells with which they are genetically associated. They may each "pay out" a strand—the subsequent axis-cylinder which keeps them in union with their mother cell. This is, of course, a mere speculation. If the sympathetic rudiments are separated off from the rudiments of the spinal ganglia as His teaches, the genetic connection would be difficult to explain, since the fibres of the white rami communicantes travel chiefly in anterior roots. At any rate the fact of migration makes the retention of connecting fibres between mother cells and daughter cells possible, whereas, if the ganglia had completely independent rudiments, it would be impossible.

The strongest argument for discontinuity of neurons in the sympathetic ganglia is to be derived from the well-known observations of Langley and Anderson, that nicotin paralyses the ganglia, preventing the passage of impulses *viâ* the ganglion-cells, while it does not paralyse the fibres which pass without interruption through the ganglia. It would seem natural to suppose that the nicotin prevents the end-branches of the higher neuron from acting upon the cell-body of the lower neuron. But, on the other hand, against this interpretation is the fact that nicotin does not thus stop the passage of impulses in the ganglia of Auerbach and Meissner in the intestine.

Langley, on this account, doubts whether these are ganglion cells in the proper sense of the term. They have, however, exactly the same histological characters as the cells of the ganglia. This is shown in figs. 841, 842, 843, 844, 845, of Kölliker's handbook. A study of these intestinal plexuses reveals their amazing richness in nerve-cells. If these cells are stations for breaking up nerve-fibres afferent to the plexus into bunches of efferent nerve-fibres for the supply of the musculature of the intestinal wall; it is not impossible that they provide a separate fibril for every muscle-cell.

If the neuron theory is true it is applicable to the sympathetic system. The evidence that this is the case is not, as yet, complete or convincing. There are, on the contrary, reasons for supposing that fibres which start from cells in the cerebro-spinal axis end in cells in the sympathetic ganglia, and that fibres from cells in these ganglia end in cells of the intestinal plexuses. If such a direct connection obtains between cell and cell, the neuron theory of the separateness and isolation of all nerve-cells breaks down.

(3) THORNS.

In papers already referred to I have called attention to the following facts :—(*a*) By varying the method of preparation, although using absolutely fresh and healthy tissue, specimens of cortical pyramids and other large cells may be obtained which in some cases are absolutely thornless, whereas in other preparations they bear thorns. (*b*) Thorns present a great variety of form. Usually they are short rods ending in knobs; occasionally they appear as filaments without knobs, two or three times as long as the knobbed rods. (*c*) In certain specimens no thorns are seen, but their place is taken by one or more minute black dots. When there are several of these dots they are always arranged in a straight line.

From these facts I draw the conclusion that the substance which has the power of fixing the chrome-salt, and, therefore, on the entrance into the tissue of silver-nitrate, of forming a silver-chrome salt which is subsequently reduced,[1] is a semi-fluid substance which surrounds and invests unstaining fibrils. The usual appearance of a rod and knob is due to the fact that at the time of fixation the semi-fluid cytoplasm of the dendrites is extruded outwards along the unstained filament which every thorn contains. Beyond a certain distance from the dendrite the film, which presumably becomes thinner and thinner the farther it is from the dendrite, collects, under the force of cohesion, into a droplet. The thorn, therefore, appears as a rod ending in a knob, because this is the form which the stainable cytoplasm assumes; but there is no ground for supposing that the supporting unstained fibril ends at the knob. If a thin wire be plunged into syrup, the viscid liquid which forms a film around the wire at the moment when it is withdrawn, runs the next moment into drops. When a thorn is replaced by a row of black dots, it seems clear that the droplets are supported upon a something which resembles the wire which supports the drops of syrup.

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[1] The nature of the reaction which occurs in the Golgi method of colouration does not seem to be generally understood. The reaction appears to be as follows :—When nerve-tissue is placed in a chromate, certain cells and fibres fix the chrome-salt. When the block is dropped into nitrate of silver, the loose chrome-salt quickly diffuses out into the silver-nitrate, which it precipitates as silver-chromate. The silver-nitrate enters the block more slowly, and wherever it finds a tissue-element which has retained the chrome-salt it combines with the chrome-salt to form an unstable subchromate of silver. Osmic acid and formalin favour the fixation of the tissue, without in any way taking part in, or interfering with, the reaction.

Thorns, therefore, are not artifacts in any proper sense of the word. They are the unstained (conducting?) fibrils surrounded for a longer or shorter distance with the cytoplasm of the dendrites, the cytoplasm alone being coloured.

This hypothesis is justified by a study of the development of thorns. In young cells, in which the cytoplasm is, relatively to the nerve-fibrils, apparently more abundant than it is in adult cells, the thorns are larger and coarser. This is conspicuously the case on the woolly-looking dendrites of the cells of Purkinje at a very early stage. It may also be noticed, as was pointed out by Athias, that when the cells of Purkinje are first recognisable, filaments appear to join their cell-bodies; whereas, *pari passu* with the growth of the dendrites, the cell-body becomes clean and free from filaments, as if the dendrites carried the connecting filaments away from the body of the cell. Figs. 27, 28, and 29 represent three very typical stages in the development of a Purkinje cell.

If this evidence be admitted, gray matter contains a scaffolding formed of an infinite number of fibrils, which place the arborisations of axons and of collaterals in connection with dendrites. Owing to the extreme tenuity of these fibrils in higher animals, no method of staining them outside the cell, in such a way that they are amenable to examination by the microscope, has yet been devised; although, as will be presently explained, Bethe seems to have stained either certain of the larger fibrils or groups of fibrils. Yet the delicate fibrils of vertebrate nerve-tissue are probably the phylogenetic successors of the coarser fibrils, which Apáthy, using chloride of gold, demonstrates in invertebrates. For the protection, nourishment, and insulation of such fibrils some "intercellular substance"—in the sense in which Nissl[1] uses the term—seems to be needed. Within the cell the fibrils are supported by cytoplasm.

If it be urged that the chrome-silver staining ought to reveal the presence of this labyrinth of primitive fibrils, it may be answered that it very frequently does do so; but all preparations in which there is evidence of the existence of an infinity of fibrils are set aside as mis-stainings. Everyone who uses the Golgi method is familiar with the blotches of black deposit, looking like a burr on a wild rose-bush, which are seen here and there in most preparations. They are set aside as "deposits" because no details of structure can be seen within them; but the fibrils which appear around the edge of the blotch are no doubt actual structures about which the deposit has occurred.

Further, it must be remembered that intracellular fibrils have been described by many observers. It can hardly be doubted that such primitive fibrils exist; and if—as there seems every reason for thinking—they are the conducting elements of the nervous system, it is much more likely that they come to the cell from outside than that they originate within the cell and its dendrites.

Since Max Schultze, in "Stricker's Handbook of Histology" (1871), described the fibrillation of the cell-body, fibrillæ have been described by H. Schultze, Flemming, Benda, Dogiel, Kronthal, Apáthy, Nissl, Held, Bethe, *et al.* No two of these descriptions exactly agree, so far as regards the size and disposition of the fibrils within the cell, and it must be admitted that it is impossible at the present moment to form a clear idea as to their nature. Bethe's[1] descriptions are the most definite. He stains the primitive fibrils with toluidin blue after solution of Nissl's bodies in ammonia. The fibrils are so closely set in the axons that it is difficult to distinguish them individually, although the fibrils destined for collaterals are recognisable owing to their greater distinctness and dark colouring. But by no means all the fibrils which join dendrites are destined for the axon. Some traverse the cell body on their road from one dendrite to another. Others again, enter by one branch of a dendrite and leave by another. Bethe's description differs from Apáthy's in one very important respect. He sees the primitive fibrils as distinct and separate fibrils, traversing the cell-body without anastomosis, whereas Apáthy finds that in the majority of cases the entering fibrils form a plexus in the periphery of the cell from which radial branches pass to the neighbourhood of the nucleus where they form a second plexus, out of which arises the, usually single, neuro-fibril of the axon. Neither Apáthy's nor Bethe's description fits in with the description of Golgi[2] of a comparatively coarse plexus in the periphery of the cell. This latter is not perhaps a very important point. From many preparations of Golgi's intracellular network which I have made, I am inclined to regard it, since it is sometimes coarser, sometimes finer, as not the demonstration of definite structural elements but a somewhat irregular deposition of silver in the "unstainable" substance of Nissl. It seems to me that the protoplasm in which the tigroids are embedded fixes the chrome-salt, and this subsequently combines with the silver, without regard to any primitive fibrils which may pass through it, except in so far as the arrangement of the fibrils determines the arrangement of the silver-reducing substance of the cells.

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[1] Nissl. "Nervenzellen und graue Substanz,' *Münch. med. Wochenschrift*, 1898, pp. 988, 1023, 1060.

With Apáthy's and Bethe's definite results before us, as well as the less certain observations of many previous observers, it is impossible to doubt that the non-staining substance of Nissl is traversed by fibrils, although we still have much to learn with regard to their thickness, course and disposition. Especially must we regard it as uncertain at present (1) whether the fibrils form a plexus within the cell or cross one another in a feltwork, and (2) whether each fibril is a distinct unit which always retains its individuality, or whether it may fuse with other fibrils. Bethe regards every fibril as an independent conducting strand, presumably incapable of fusion with other fibrils. Apáthy sees the fibrils unite to form thicker fibrils and subdivide into finer fibrils.

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[1] Bethe. "Ueber die Primitivfibrillen in den Ganglienzellen vom Menschen, &c." *Schwalbe's morphologische Arbeiten*, viii., 1898, p. 95.

[2] Golgi. "Sur la structure des cellules nerveuses." *Archives ital. de biol.*, xxx., 1898, p. 60.

Accepting Bethe's description of fibrils, it is to be noted that he observes them entering and leaving the dendrites by their *branches* only. Here I venture to think that Bethe's observations are incomplete. It appears to me that no account of the minute anatomy of the nerve-cell is satisfactory which ignores the "thorns." Thorns as shown by chrome-silver colouration are most definite structures of obvious physiological importance. From Bethe's figures and description I gather that his staining method does not reveal their presence, and this being the case, I take it that his stain fills in a part of the picture only. The arguments already used lead me to the conclusion that *every thorn is a fibril near its junction with a cell.* Apáthy's and Bethe's "primitive fibrils" may be bundles of fibrils, or they may be fibrils formed by the fusion of a number of truly primitive fibrils—"elementary fibrils," as Apáthy terms them—but the combined fibrils are not properly entitled to be styled primitive. Every thorn is the cell-end of a primitive fibril. Probably the true primitive fibrils fuse to form the fibrils which Apáthy recognises, when stained with chloride of gold, in the same way as Apáthy's elementary fibrils unite into his "primitive fibrils," and then fuse again to form "neurofibrils."

In one of the papers already referred to I have hazarded the conjecture that nerve-conduction depends upon the establishment of a certain relation between the conducting fibrils and the cell-protoplasm by which they are invested.

I have endeavoured to show that if this be the case, all the phenomena of attention, inhibition, sleep, which have been supposed to have their physical basis in the condition of extension, to a greater or less extent, of pseudopodial processes of the dendrites, might be just as well explained as the result of the extension along the conducting fibrils, to a greater or less extent, of the cytoplasm. My hypothesis, indeed, removes a fundamental difficulty in the conduction-by-contact theory. Upholders of this theory speak of the extension of processes from one neuron to another as a natural physiological precursor of conduction. They talk of "conduction by contact" as if it presented no physical difficulties. They forget that at the time when an impulse has traversed the neuron A on its way to the neuron B, the approximation of the conducting processes of the two neurons can be effected by no means other than the *passage across the gap* which separates them of the impulse which is about to be conducted along a physiologically continuous strand. *Conductio in distans* must precede conduction by contact. In other words, the contact theory does not in any way explain the antecedent adjustment by which contact is brought about. Now, my hypothesis of continuity of the conducting filaments, with variability of their effectiveness as conductors, gives a more intelligible explanation of "attention" and "inhibition." The conducting fibrils never lose a low degree of conductivity. The first impulse which struggles through from nerve-cell A to nerve-cell B brings about an overflow of cytoplasm from the one to the other which, *ipso facto*, creates an open road along which subsequent impulses—all impulses are, of course, vibratory—pass with ease. At the same time other paths, not in the circuit, are blocked by withdrawal of cytoplasm; producing the well-known phenomenon of inhibition for all competing reflexes.

This hypothesis also disposes of what has been termed the "physiological evidence in favour of the neuron theory." Physiologists have resisted the doctrine of the continuity of conducting fibrils, on the ground that such continuity leaves the nerve-cells nothing to do—gives no opportunity for the explanation of the tiring of nerve-cells, the delay of impulses, &c. But if effectiveness of conduction depends upon a certain relation between the conductor and the cytoplasm in which it is embedded, it is free to the physiologists to restore to the nerve-cells any prerogatives which they may consider that their status in the system requires.

We can imagine that some day the quality of all nerve phenomena, from a knee-jerk to a thought, will be explained as due to the distribution of sensory impressions through the labyrinth of fibrils, the conductivity of which is automatically regulated by the impulses themselves, within the limits imposed by the hereditary tendency of the individual's cytoplasm to overflow in certain directions, and with certain urgency, and the functional condition of the cytoplasm at the time; but until my hypothesis has some basis on histological observations it is futile to consider the more detailed applications which may be made of it.

Lastly, not all kinds of cells bear thorns. In the case of the cerebellum, for example, it is remarkable that whereas the superficial molecular cells, Cajal's cells, and Purkinje's cells are conspicuous for their thorniness, the cells of Golgi have thornless dendrites. As the cells of Golgi are indubitably nervous, the absence of thorns cannot be without significance; and one naturally notes that these cells are remarkable for the extreme richness of the branching of their axis-cylinders. Their elaborate arborisation provides a complicated system of intercommunication with other nerve-cells or fibres, without any need for the dendrite system to be called into play, to the same extent as in the cells of Purkinje for example. We may suppose that, in the case of Golgi's cells, the collection of fibrils from afferent nerves does not, as in the case of other cerebellar cells, occur chiefly through the dendrites. Hence the dendrites are not studded with the ends of entering fibrils, *i.e.*, there are no thorns.

THE CONNECTION OF DENDRITES WITH CONNECTIVE TISSUE ELEMENTS.

As is well-known the continuity of dendrites with pia mater and with blood-vessels was described by Golgi and

Rámon y Cajal. If the chrome-silver method is to be trusted such a connection is beyond dispute. The apical processes of developing granules are seen to end in knobs beneath the pia mater, and the connection of dendrites with connective tissue elements is in certain cases unmistakable. The dismissal of such connections as occasional does nothing to clear the ground. If it ever obtains, and it is difficult to suppose that the definite silver colouration occurs in the absence of any underlying substance, it is a matter of profound significance, for it compels the conclusion that the dendrites are not solely composed of conducting substance. They must consist of a non-conducting cell-substance which fuses with, or at any rate reaches to, the connective tissue elements, and of conducting substance, presumably fibrils, which does not extend to the tips of the dendrites. We must figure the cytoplasm as forming dendrites through which conducting fibrils pass. Provided the fibrils are isolated from the connective tissue it matters little whether the rest of the cell substance is connected with it or no. Rohde[1] described the continuity of the spongioplasm of nerve-cells with the spongioplasm of connective tissue cells in the electric lobe of Torpedo, whereas the hyaloplasm of the nerve-cell is distinct. He had not observed primitive fibrils.

SUMMARY.

The neuron theory, or statement, alleges the anatomical independence of nerve-cells.

This statement is based upon appearances obtained by methods which colour the cytoplasm and leave the conducting elements uncoloured.

(1) Even in chrome-silver preparations evidence is forthcoming that fibres which start as the axons of certain larger cells end, after subdivision, by uniting directly with smaller cells. Such a connection of cell with cell is to be seen or inferred in the case of (*A*) the granules of the cerebellum and in (*B*) of the cells of the sympathetic system.

(*A*) If the granules of the cerebellum are observed in their embryonic condition—when they are carrot-like and as yet unfurnished with clawed arms—they are seen to be directly connected with fibres from the arbor vitæ. (*a*) The same fibre from the arbor vitæ may divide to form the axons of two or more granules. (*b*) A granule which gives the characteristic divaricating axon to the molecular layer may, in addition, send an axon to the arbor vitæ.

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[1] Rohde. *Arch. f. mikros. Anat.*, 1895, p. 408.

(*B*) There are reasons for concluding that the slender processes of cells of the sympathetic system (which are universally regarded as dendrites) are in reality axons or nerve-fibres. If this be correct each cell receives the axon of a cell higher in the system and gives off a bunch of finer axons for cells lower in the system—is, in fact, a distributing cell.

(2) Thorns are in no sense artifacts, but primitive fibrils invested by cytoplasm for a certain distance from the dendrites into which they enter. Since the cytoplasm is continued but a short distance along the fibrils, and since this substance is alone coloured by the methylene-blue or the chrome-silver methods, the cell-end of the fibril appears as a thorn, or rather as a rod with a knob (gemmule), owing to the semi-fluid sheath of cytoplasm having collected at its end into a droplet.

DESCRIPTION OF FIGURES.

In most of the figures the positions of the cells of Purkinje and of the fibres of the arbor vitæ are indicated. Their size and the distance between them shows the magnification.

PLATE 1.

FIG. 1.—Puppy, 6 days old. Cerebellum. Hardened in bichromate of potassium and osmic acid mixture for more than a year. Two granules with axis-cylinder processes which divaricate in the molecular layer and, in addition, slender processes passing to the arbor vitæ which have the appearance of axis-cylinders.

FIG. 2.—Kitten, 4 days old. Cerebellum. Hardened six months. A granule giving an axis-cylinder to the molecular layer and another to the arbor vitæ.

FIG. 3.—Same preparation as fig. 1. The fibre to the arbor vitæ gives off branches at right angles.

FIG. 4.—Same preparation as fig. 2. The fibre to the arbor vitæ is not so directly continuous with the granule as in figs. 1 and 2. It looks as if some sort of basket or "claw" connection were being formed.

FIG. 5.—Same preparation as fig. 2. Shows the same method of connection of a fibre from the arbor vitæ with a granule.

PLATE I.

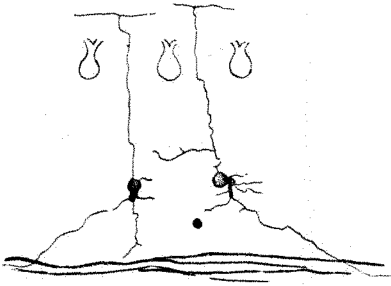

FIG. 1.

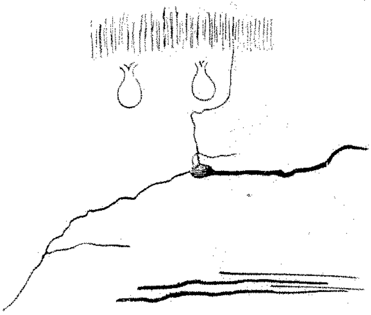

FIG. 2.

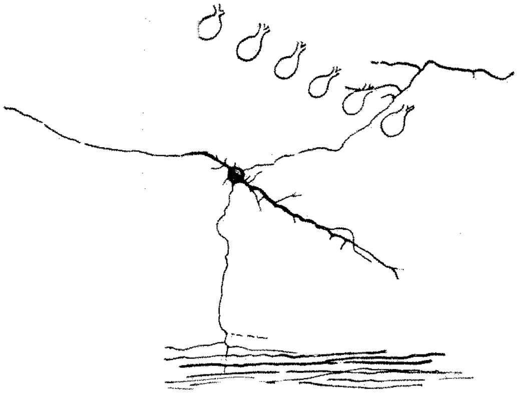

FIG. 3.

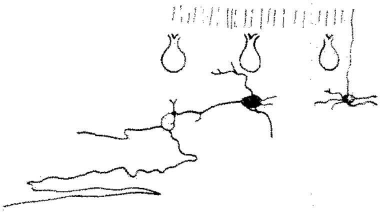

FIG. 4.

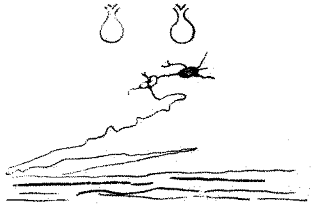

FIG. 5.

PLATE II.

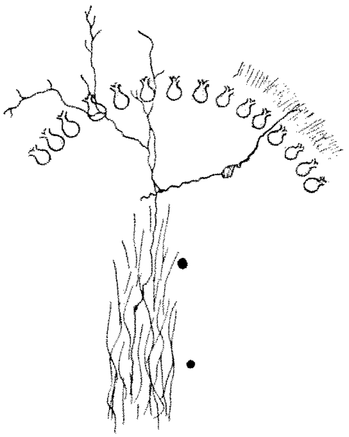

Fig. 6.

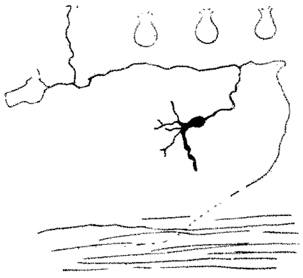

Fig. 7.

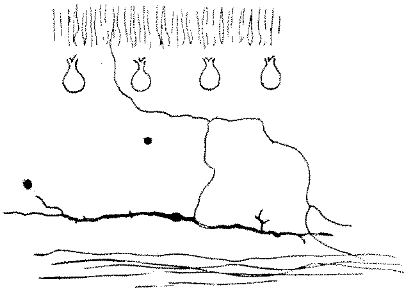

Fig. 8.

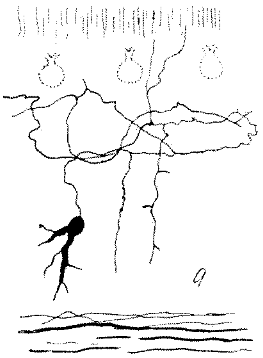

Fig. 9.

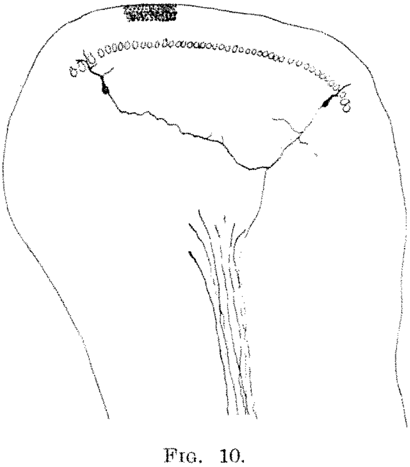

Fig. 10.

PLATE III.

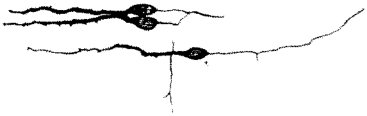

FIG. 11.

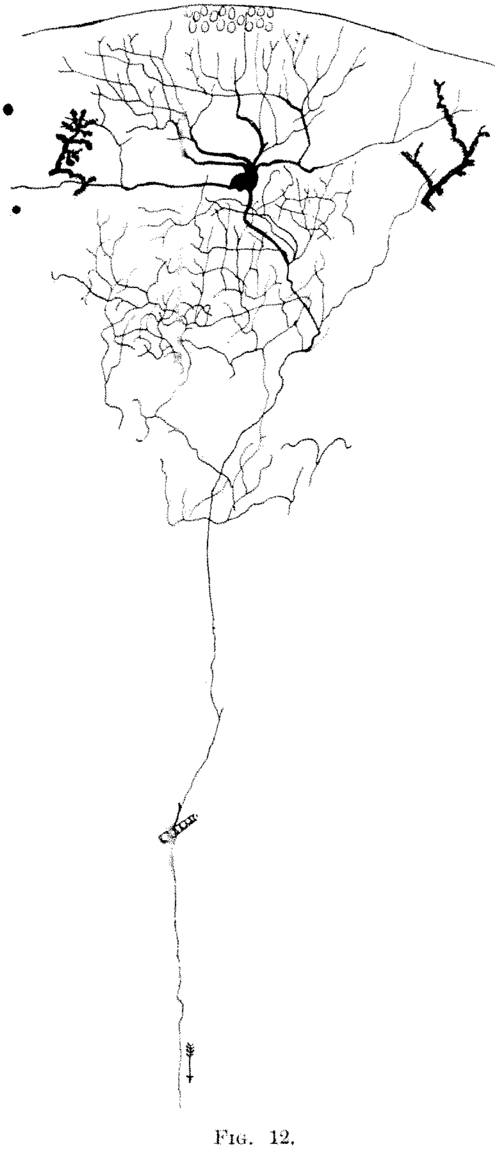

FIG. 12.

PLATE IV.

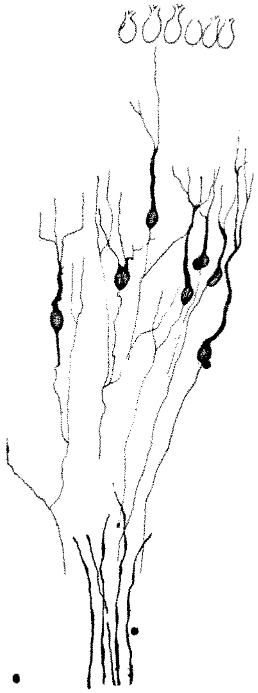

FIG. 13.

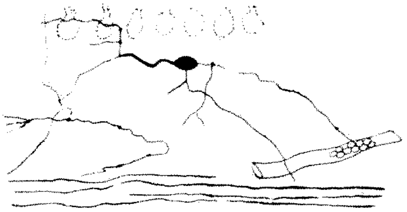

FIG. 14.

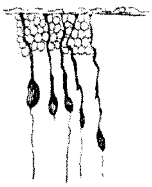

FIG. 15.

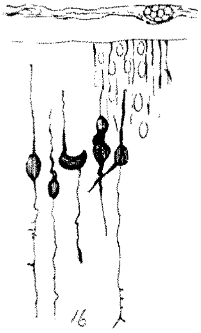

FIG 16.

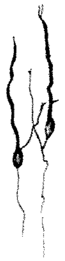

FIG. 17.

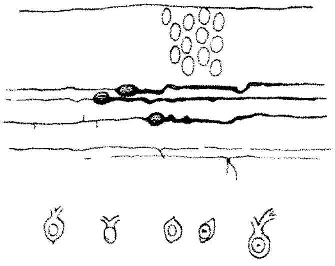

FIG. 18.

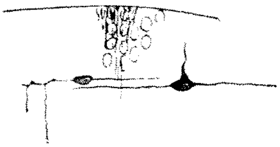

FIG. 19.

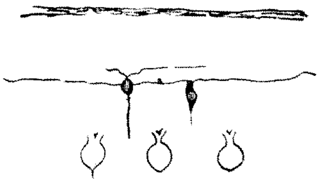

FIG. 20.

PLATE V.

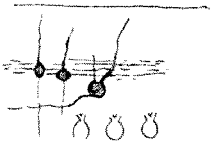

FIG. 21.

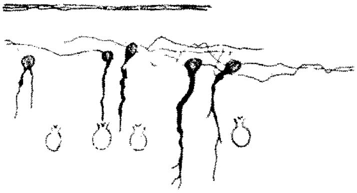

FIG. 22.

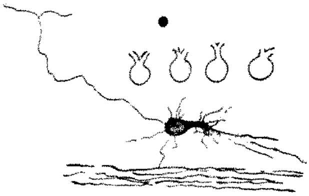

FIG. 23.

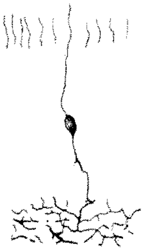

FIG. 24.

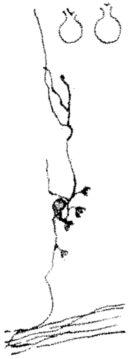

FIG 25.

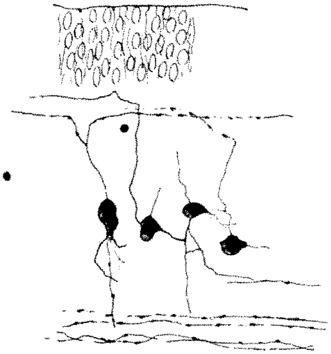

FIG. 26.

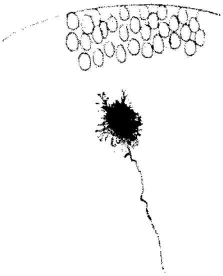

FIG. 27.

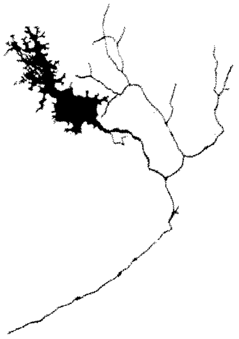

FIG. 28.

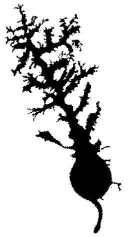

FIG. 29.

PLATE 2.

FIG. 6.—Same preparation as fig. 2. A granule which shows a curiously thick process passing between the cells of Purkinje into the molecular layer, and a centripetal axon which appears to join a fibre which branches in the molecular layer.

FIG. 7.—Same preparation as fig. 2. The axon of the granule divides into one branch which passes backwards to the arbor vitæ and another branch which again gives off a branch before it enters the molecular layer.

FIG. 8.—Rat, 12 days old. Cerebellum hardened in bichromate of potassium and osmic acid for twelve months. The granule, which lies near to and parallel with the fibres of the arbor vitæ, gives off an axon which divaricates before it has passed the layer of cells of Purkinje, one of the two branches entering the molecular layer and the other returning towards the arbor vitæ.

FIG. 9.—Kitten, 10 days old. Hardened six months. A granule, the axon of which has a very complicated and tortuous course before it gives a branch which bifurcates on its way to the molecular layer.

FIG. 10.—Kitten, 4 days old. Two carrot-granules at opposite sides of the folium are provided with axons which unite into a single fibre which can be followed for a considerable distance in the arbor vitæ. The nuclei of Obersteiner's layer are shown at one place beneath the pia mater.

PLATE 3.

FIG. 11.—Kitten, 7 days old. Hardened for two months. Two granules with united axons.

FIG. 12.—A single Golgi-cell is seen lying between two fragments of the thorny dendritic systems of Purkinje-cells at the apex of a folium. The dendrites of the Golgi-cell are thornless. The axon of the cell, after giving rise to a copious arborescence, is continued to the very base of the folium, a distance of at least 2 mm.

PLATE 4.

FIG. 13.—Kitten, 1½ days old. Hardened nine months. The section, which cuts the folium transversely, passes obliquely through the granular layer, from the cells of Purkinje to the arbor vitæ. It shows a very typical group of carrot-granules. The axons of some of the granules are unbranched, others give off collaterals.

FIG. 14.—Kitten, 7 days old. Hardened in bichromate of potassium and osmic acid for nearly two years. The cell, which is rather larger than an ordinary granule, gives off three processes, each of which has the character of an axon.

FIGS. 15, 16, 17.—Kitten, 4 days old. Three groups of cells placed vertically to the pia mater, which appear to be developing carrot-granules. Figs. 15 and 17 with obj. ⅓ in., oc. 4; fig. 16, obj. ⅛ in., oc. 8.

FIG. 18.—Kitten, 17 days old. Section parallel to long axis of folium; oblique to surface. In the molecular layer just below Obersteiner's layer (superficial granular layer) are three cells lying parallel to the surface. The distinction between the apical process and the axon is marked with unusual clearness; but every intermediate form is to be observed between such cells as these and cells which appear to give off a long axis-cylinder process on either side. The axon of the deepest of the three cells gives short lateral branches. The divaricating fibres into which the axons of granules divide are seen beneath the three "fibre-cells."

FIG. 19.—Kitten, 17 days old. Two tangential cells in the molecular layer, immediately beneath Obersteiner's layer. The cell to the right shows an apical process directed towards the surface.

FIG. 20.—Kitten, 17 days old. Two granules in an early stage of development. They lie in the molecular layer just beneath Obersteiner's nuclei. According to Rámon y Cajal's account they have been formed by the pinching together of the processes of tangential cells similar to those shown in figs. 18 and 19.

PLATE 5.

FIG. 21.—Kitten, 4 days old. Cells in molecular layer just beneath tangential cells of an ambiguous character—apparently developing carrot-granules.

FIG. 22.—Kitten, 1½ days old. Developing granules the apical processes of which reach as far as, or beyond, the cells of Purkinje.

FIG. 23.—Puppy, 6 days old. A granule in a more advanced condition. The apical process is carrot-shaped with large numbers of slender branches. It lies almost parallel to the fibres of the arbor vitæ. Its axon bifurcates in the molecular layer.

FIG. 24.—Hedgehog, 2 weeks old. The apical process appears to join one of the branches of a "mossy" fibre. This is typical of a large number of preparations in which a direct union between a mossy fibre and the apical process of a developing granule can be traced.

FIG. 25.—Hedgehog, 2 weeks old. A granule which still shows an apical process extending into the arbor vitæ as well as an axon which enters the molecular layer; but it also exhibits commencing arms with claws. Figs. 20, 22, 23, 24, 25 represent successive stages in the development of granules, intermediate between the tangential "fibre-cell" and the adult round granule with five or six clawed arms.

FIG. 26.—Kitten, 2 days old. Four granules which lie in the granular layer. Each gives a characteristic axon to the molecular layer, and, in addition, several slender processes towards the arbor vitæ. The processes of the two middle granules appear to unite together.

FIG. 27.—Kitten, 1½ days old. A young Purkinje-cell which has not yet developed a dendritic system. A multitude of fibrils appear to enter the body of the cell.

FIG. 28.—Hedgehog, between 2 and 3 weeks old. A young Purkinje-cell, the dendritic system of which has begun to develop. The body of the cell has fewer fibrils connected with it than in fig. 27.

FIG. 29.—Puppy, 6 days old. The dendritic system is more developed than in fig. 28. The body of the cell is almost free from fibrils. A somewhat more advanced Purkinje-cell. The thorns in the last two specimens are much larger and coarser than they are in the adult.

A CASE OF VIVID AFTER-IMAGES EXPLAINED ON HERING'S THEORY.

BY DAVID FRASER HARRIS, M.D., B.SC.(LOND).

Lecturer on Physiology in the University of St. Andrews.

THE phenomena recorded and analysed below were experienced by myself when I was occupied in estimating the principal focal lengths of one or two convex lenses.

While focussing the sun's rays at noon upon a sheet of white paper, and without at the moment thinking of the probable effect on the retina, I stared at the dazzlingly white spot for some time, until roused by noticing that the paper was on the point of being set on fire.

On turning my eyes towards the least well-lighted corner of the white-walled room, I noticed a most pronounced black after-image, which persisted for about thirty seconds. Had this merely faded away and given place to normal colour-vision, there would have been nothing more to be experienced than the familiar sensation of being "blinded" as after gazing at the sun itself; but the black patch was followed by two coloured images of such brilliance and, *pro tem.*, apparently so persistent, that a record of them may be pardoned.

The first was a beautiful rose-pink patch, referable to the part of the retina concerned in direct vision; it lasted about three minutes; it was replaced by a brilliant canary-yellow patch of rather larger size, persisting for about twice as long. Before this last had faded I had to leave the building, and so experienced the very unusual sensation of seeing, almost as through a piece of yellow glass, all objects projected on the central portion of the retina; while at the same time their colours seemed less changed than if yellow glass had really been used.

It seems to me that Hering's theory of colour-vision accounts for the colours of these after-images, and for their order of succession.

The theory virtually involves the following (for light of ordinary intensities) :—

(1) That white light katabolises the white-black substance,[1] and the vision of a black object (or darkness) anabolises it; but further, that each coloured ray, *i.e.*, of homogeneous light, katabolises the W.-B. Sb., so that whatever other (chromatic) effects it may have, each *coloured* light gives rise to a certain amount of the sensation of white—to a very different degree for the various rays, yellow doing so most of all—hence, as Foster[2] remarks, "a fully saturated colour . . . . . according to this view does not exist."

(2) That katabolism of the red-green substance[3] gives rise to a sensation of red, anabolism of it, of green; that if there is metabolic equilibrium (as under the influence of spectral yellow) there is neither red nor green since opposite tendencies are neutralised, but that if any katabolism predominates over any co-existing anabolism, the sensation will tend towards "orange"; if anabolism predominates, the sensation will tend towards a greenish hue.

(3) Similarly for the yellow-blue substance;[4] katabolism alone gives yellow, anabolism blue, a predominance of the one a yellowish, of the other a bluish hue; while spectral green leaves it in metabolic equilibrium.

Thus the various homogeneous constituents of heterogeneous (white) light are supposed to simultaneously affect the several hypothetical visual substances in such a fashion that the tendencies to katabolism are just balanced by those to anabolism, and hence no *chromatic* sensations result—at least not with diffuse light of ordinary intensity; but it must be somewhat different with sunlight of such unusual brilliance as to temporarily "blind" the retina (produce the black negative after-image).

With such light there are, in fact, present the conditions to ensure, on the whole, a marked excess of katabolism over anabolism, and seeing that in noonday sunlight there is a relative predominance of such rays as are associated with maximal luminosity, viz., the orange-yellow, the first effect in consciousness would be a sensation of white so intense as to render for a time any concomitant chromatic sensations unperceived.

Violent katabolism has been set up in the R.-G. and Y.-B. substances, and will make itself felt in consciousness as soon as the negative after-image of black (resulting from the rapid reconstitution of the W.-B. Sb. on the cessation of the very violent stimulation) has passed away.

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[1] W.-B. Sb.

[2] "Text-book of Physiology," part iv., 6th ed., p. 1349.

[3] R.-G. Sb.

[4] Y.-B. Sb.

The first effect is that of a rose-pink patch from the katabolism of the R.-G. Sb. by the orange rays, virtually a positive after-effect due to retino-cerebral functional inertia. It is pink and not a pure or saturated red because, *ex-hypothesi*, there is always some concomitant katabolism of the W.-B. Sb. along with any effect due to coloured rays. As soon, however, as the metabolic equilibrium of the R.-G. Sb. has been re-established, a yellow patch is perceived due to the predominance of katabolism over anabolism in the Y.-B. Sb. We have experimental evidence[1] that, as studied under appropriate conditions, the sensation of red is elicited in a shorter time than that of green, and still more so than that of violet; in other words, yellow takes a longer time to be developed than red.

Thus, as the red sensation passes off, the yellow is reaching its maximum,[2] the katabolic phase in the Y.-B. Sb. long out-living the period of action of the stimulus which produced the disturbance. The yellow is now the only chromatic sensation not neutralised, and it is perceived in its fulness until, on the metabolic equilibrium being re-established, it, too, fades away, and the retina recovers from its state of over-stimulation.

Review.

Neurypnology, or the Rationale of Nervous Sleep, considered in Relation to Animal Magnetism or Mesmerism and Illustrated by Numerous Cases of its Successful Application in the Relief and Cure of Disease. By JAMES BRAID, M.R.C.S., C.M.W.S., &c. A new edition, edited with an introduction, biographical and bibliographical, embodying the author's later views and further evidence on the subject, by ARTHUR EDWARD WAITE. London, George Redway. 1899.

THE above work comprises (1) a biographical introduction, which gives a short account of Braid's life and a more extended one of his writings; (2) a reproduction of the original edition of "Neurypnology," which forms the greater part of the volume; (3) an appendix of editorial notes chiefly drawn from Braid's later works; and (4) a bibliography of Braid's writings.

According to Mr. Waite, little is known about Braid in this country, and there is no trustworthy bibliography of his writings.

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[1] Stewart, *P.R.S.E.*, 1888, p. 441.

[2] It has a slightly greater degree of functional inertia.

His later works, rare and almost unknown, have been traced with difficulty. Mr. Waite, however, claims to have been successful in his researches, and presents, as their result, a work on Braid which he asserts to be substantially complete.

Mr. Waite has undoubtedly rendered a service to hypnotic literature, but he has not made the most of the material collected, and his work is neither as complete nor as accurate as he believes it to be. The following are a few, amongst many, objections which might be urged against it: Thus, we are told that the discovery of hypnotism alone lifted Braid out of the groove of the ordinary practitioner. This is incorrect. Before he discovered hypnotism Braid had operated on 262 cases of talipes, 700 cases of strabismus, and twenty-three cases of spinal curvature, and his reputation as a surgeon attracted patients from all parts of the country.

Although "Neurypnology" is historically interesting, it must not be forgotten that it was written almost immediately after Braid commenced hypnotic work, and that later his views underwent a complete change. The French translation of "Neurypnology" is more valuable than Mr. Waite's, as in an appendix of thirty-six pages it gives a full translation of Braid's last manuscript, containing a summary of his more matured theories. This is barely referred to by Mr. Waite.

Some passages show a somewhat unusual want of care in compilation. Thus (pages 317-319), a case of torticollis cured by suggestion is recorded at length, and we are told that a year later there had been no relapse. The case is repeated (pages 343, 344) along with the fresh statement that "whether the cure was permanent does not appear from the narrative."

The bibliography, to which Mr. Waite attaches great importance, only imperfectly reproduces those I myself published at earlier dates (BRAIN, part lxxiii., Spring, 1896; *Proceedings of the Society for Psychical Research*, part xxx., June, 1896; *Revue de l'Hypnotisme*, June, 1898). In seven of the works referred to by Mr. Waite the title is wrong or incomplete; in twenty-one, quoted from medical journals, neither volume nor page is given. The only new material is two unimportant letters in reply to one from "James Simpson, Esq., advocate," erroneously described by Mr. Waite as "James Singer," while in my bibliographies are to be found nine of Braid's writings which are omitted from Mr. Waite's. Further, some of Braid's works, of which Mr. Waite has been unable to trace a single copy, have long been in my possession.

According to Mr. Waite, Braid's connection with the debated subject of phrenology terminated with the phreno-hypnotic experiments recorded in "Neurypnology." The subject, we are told, remains where he left it, while Dr. Foveau de Courmelle's verdict, viz., that the phenomena are as likely to be the result of real action as of unconscious suggestion, is accepted by the unprejudiced. Mr. Waite is ignorant of, or ignores, Braid's later experiments. From these Braid concluded that all phrenological phenomena were the result of direct or indirect suggestion, and arose either from a previous knowledge of phrenology or from a system of training during hypnosis. They manifested themselves when points were touched, which audible suggestion had taught the subjects to associate with particular ideas. Further, pressure upon the head was not necessary, and the associations could be established in the same artificial way between the phenomena and other parts of the body. Finally, the excitation of the muscles of expression was capable of arousing corresponding ideas in the subject's mind.

It is certainly surprising to be told at the present day that the phenomena of phrenology are as likely as not to be genuine.

Mr. Waite's account of Braid's views on mesmerism or animal magnetism demand serious notice. Formerly, according to him, it was generally but erroneously believed that Braid opposed animal magnetism. Thanks. however, to French writers this error has been rectified. Braid was the champion and witness of animal magnetism, and placed the central fact of mesmerism beyond all further dispute. In opposition to this it is to be noted, and the point cannot be too strongly insisted upon, that the primary and cardinal fact on which Braid founded all his theories of hypnotism was the purely subjective origin of its phenomena. Everything depended on the physical and mental condition of the patient; not on the volition or passes of the operator which threw out magnetism, or called into action some occult fluid or medium. Braid never swerved from this view. Later, he repeated it more emphatically, and demonstrated experimentally that all the phenomena attributed to magnets, metals, drugs in sealed tubes, &c., could be equally well produced by direct or indirect suggestion when the supposed exciting agents were absent. Thus, a wooden magnet acted like a real one when the subject was deceived as to its nature, whereas a genuine one produced nothing if the subject did not know it was there.

According to Waite, "the metalo-therapeutic theory, first discovered by Burq and developed by Charcot, inaugurated a new era of hypnotism, and led to that long series of researches connected with the Salpêtrière School of Paris, which have done so much to obscure, if not, indeed, to tarnish, the rival lustre of the Nancy School of Liébault."

This view of metallo-therapeutics is many years too late. The opinions of Burq, which were shared by Elliotson and the mesmerists of his day, were successfully combated by Braid. Charcot simply revived an ancient fallacy, which the Nancy School, following in Braid's footsteps, again overthrew. As far back as the International Congress of Psychology of 1892, the Charcot theories had practically ceased to excite scientific interest.

The assertions of the mesmerists as to the clairvoyant powers of their subjects were described by Braid as opposed to all that was known of physical science. The following, he said, were frequent sources of error in clairvoyant experiments:—(1) The hyperæsthesia of the organs of special sense, which enabled impressions to be perceived through the ordinary media that would pass unrecognised in the waking condition. (2) The docility and sympathy of the subjects, which tended to make them imitate the action of others. (3) The extraordinary revival of memory by which they could recall things long forgotten in the waking state. (4) The remarkable effect of contact in arousing memory. (5) The condition of double consciousness or double personality. (6) The vivid state of the imagination, which instantly invested every suggested idea, or remembrance of past impressions, with the attributes of present realities. (7) The tendency of the human mind, in those with a great love of the marvellous, to erroneously interpret the subject's replies in accordance with their own desires. (8) Deductions rapidly drawn by the subject from unintentional suggestions given by the operator.

According to Braid, the belief in thought-transference was also the result of careless experiment, and he had never met with a subject who could divine his thoughts when their transmission by the recognised media had been rigorously excluded.

Braid did not believe that mesmeric subjects possessed intuitive powers. Doubtlessly some of them successfully predicted their own hysterical attacks, but the prophecy simply produced its own fulfilment through self-suggestion.

According to Mr. Waite, "it has been rightly observed that Braid, the discoverer, so to speak, of suggestion, by no means realised the possibilities of suggestion of the unconscious kind." Bernheim, and other writers unacquainted with Braid's later works, had previously made similar statements. It is difficult, however, to understand how Mr. Waite could commit a similar error. Braid repeatedly, clearly, and emphatically pointed out that unconscious suggestion accounted for all the phenomena which the mesmerists attributed to magnets, metals, and occult fluids. Sometimes, he said, the suggestions were given in their most obvious form by the operator verbally predicting in the subject's hearing the nature of the phenomena which ought to appear; At others they were given less directly by passes, manipulations, excitation of the muscles of expression, &c.; but these owed their power, not to their physical influence, but to the ideas they excited in the subject's mind. When all forms of suggestion were rigorously excluded, the mesmeric phenomena did not appear. This, Braid asserted, proved the influence was a mental one; were it electric, suggestions were as unnecessary in the case of the subject as in that of a galvanic battery.

Apparently Mr. Waite believes in animal magnetism, metallotherapeutics, phrenology, and clairvoyance. All these things Braid successfully combated, and to attribute to him any belief in their existence shows an absolute failure to grasp the spirit and significance of his teaching.

J. Milne Bramwell.

Rules

AND

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OF THE

Neurological Society of London,

1900.

WITH THE

Annual Report of Council, and Balance Sheet for the Year 1899.

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Neurological Society of London.

REPORT OF COUNCIL.

FEBRUARY 8, 1900.

The Council has much pleasure in reporting the continued success and prosperity of the Society. The members now number 216.

The Inaugural Address was delivered at the Annual General Meeting on February 2nd, 1899, by Dr. W H. GASKELL. F.R.S., on "The Meaning of the Cranial Nerves."

Sir SAMUEL WILKS, Bart., F.R.S., the second President of the Society, has been elected an Honorary Member.

During the summer the Society met out of London for the second time since its constitution, and as on the former occasion, the Meeting was held in the Physiological Department at Cambridge, where Dr. RIVERS and Mr. MYERS made communications on the "Psychology of the Natives of Borneo and Torres Strait."

In response to an invitation from the Secretaries of the Section of Neurology at the Thirteenth International Congress of Medicine, to be held in Paris, in 1900, Dr. DAVID FERRIER, F.R.S., and Dr. C. S. SHERRINGTON, F.R.S., have been nominated to represent the Society at that Congress.

As has now become the custom, the Proceedings of the Society have been published at some length in "Brain," and an abstract appended to this Report shows the value and character of the work that has been done during the year.

Proceedings of the Society during the year 1899.

February 2nd, Dr. W. H. **Gaskell**, F.R.S, Inaugural Address, "The Meaning of the Cranial Nerves."

March 2nd, Dr. **Stansfield**, "Epileptic Insanity associated with Mastoid Disease; operation; improvement of mental symptoms." Dr. F. E. **Batten**, "Unusual Form of Muscular Atrophy in a Boy." Dr. **Caley**, "Case with Symptoms of Syringo-myelia with Sudden Increase followed by Sudden Diminution in Intensity." Dr. **Wilfred Harris**, "Hæmorrhage into the Cord. Dr. J. H. **Bryant**, "Tremors of Hand like those of Paralysis Agitans, following Typhoid Fever." Dr. **Tooth**, "Peroneal Type of Muscular Atrophy."

May 11th, in the Physiological Laboratory at St. Mary's Hospital, Dr. **Waller**, F.R.S., Demonstration of the Action of Veratrine, Betaine, Neurine, Choline, Muscarine, Snake Venom, and Tetanus Toxin on Isolated Nerve. Professor E. A. **Schäfer**, F.R.S., Microscopic Sections illustrating (1) Termination of the Fibres of the Pyramidal Tracts of the Cord; (2) Origin of the Fibres of the Dorsal and Ventral Cerebellar Tracts of the Cord.

June 17th, at the Physiological Laboratory, Cambridge, Dr. W. H. R. **Rivers** and Mr. **Charles S. Myers**, "Some Psychological Observations on the Natives of Torres Straits and Borneo."

October 26th, Dr. J. A. **Coutts** and Dr A. M. **Gossage**, "Unusual Case of Paralysis of Acute Onset." Dr. **James Collier**, "A Case with Acute Onset resembling Friedreich's Disease.' Dr. **James Collier**, "Case of Myopathy of Laudouzy-Dejerine Type." Dr. **Wilfred Harris**, "Case of Myopathy of Landouzy-Dejerine Type." Dr. C. E. **Beevor**, "A Case of Cerebral Degeneration (Diplegia)."

December 7th, Dr. F. E. **Batten** and Dr. J. S. **Collier**, "Spinal Cord Changes in Cases of Cerebral Tumour."

December 21st (Adjourned Meeting), Mr. **Victor Horsley**, F.R.S., "Brown-Séquard Fits in a Cat." Dr. **Wilfred Harris**, "An Experimental Investigation on the Decussation of the Optic Nerves in various Animals, and on the Path of the Reflex for the Contraction of the Pupil to Light."

BALANCE SHEET, 1899.

Cr. NEUROLOGICAL SOCIETY. Dr.

RECEIPTS.

	£	s.	d.
To Balance	65	16	2
Subscriptions	200	6	0
Half Share of profit on "Brain" ...	54	8	4
Contribution by Messrs. Macmillan towards cost of Illustrations in "Brain"	18	0	0
	£338	10	6

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Pulman & Son	2	3	0			
Bale & Danielsson ...	16	5	11			
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Audited and found correct December 6, 1899,

W. T. Holmes Spicer,
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RULES.

1.—The Society shall be called the NEUROLOGICAL SOCIETY OF LONDON.

2.—The objects of the Society shall be to promote the advance of Neurology and to facilitate intercourse amongst those who cultivate it, whether from a Psychological, Physiological, Anatomical, or Pathological point of view.

3.—The Society shall consist of Ordinary, Corresponding, and Honorary Members.

4.—Any one engaged in researches bearing on Neurology, or manifesting interest in such researches, shall be eligible for the Ordinary Membership.

5.—Men of distinction in Science, who have contributed to the advancement of Neurology, shall be eligible for the Honorary, or for the Corresponding Membership.

6.—The number of Honorary Members shall be limited to six, and that of Corresponding Members to twelve.

7.—Honorary and Corresponding Members shall have the right of attending the Meetings of the Society and of taking part in them.

8.—Honorary and Corresponding Members shall be elected by the Society on the recommendation of the Council.

9.—Candidates for Ordinary Membership shall be recommended by at least three Members of the Society, who shall append their names to a printed form supplied by the Secretaries to any person seeking Membership.

10.—The Council shall nominate candidates for election into the Society as Ordinary Members from among persons so recommended.

11.—The names of Candidates nominated by the Council shall be submitted to the next Meeting of the Society, and shall be balloted for at the next subsequent meeting, one black ball in ten excluding.

12.—The Annual Subscription of an Ordinary Member shall be One Pound, due in advance.

13.—The Treasurer shall send to each Member, shortly before the Annual General Meeting, a notice reminding him that his Subscription becomes due on that day.

14.—Non-payment of the Subscription within twelve months after it is due, shall be considered as equivalent to resignation.

15.—The Council shall consist of a President, two Vice-Presidents, two Secretaries, one Treasurer, and ten Councillors.

16.—Five Members of the Council shall form a quorum.

17.—The office of President shall be tenable for one year, and be entered upon at the beginning of each year by the Senior Vice-President.

18.—The office of Vice-President shall be tenable for two years; one Vice-President being elected every year.

19.—The Secretaries and Treasurer shall be elected annually with eligibility for re-election.

20.—The Councillors shall be elected for one year, and not more than eight shall be eligible for re-election to the same office during the following year.

21.—One full week before the Annual General Meeting, the Secretaries shall send to each Member a balloting paper containing the names of the Officers and Councillors whom the Council nominate for the ensuing year.

22.—The Society shall elect the Council by ballot, each Member, however, being at liberty to substitute other names for any of those upon the list.

23.—There shall be six Ordinary Meetings annually, of which the first held in each year shall be the Annual General Meeting.

24.—Notices of each meeting, and of the subjects to be considered, shall be sent by the Secretaries to each Member of the Society at least one week before the meeting.

25.—Special Meetings shall be held at the option of the Council, or at the request, in writing, of twenty Members.

26.—The President shall have the power of inviting any person to attend and to take part in the scientific work of the meeting.

27.—If at any time the Council shall be of opinion that the interests of the Society require the expulsion of a Member, they shall submit the question to a special General Meeting, at which, if more than one-half of the Members of the Society vote, by ballot as usual, for the expulsion of the Member, his subscription for the current year shall be returned to him, and he shall thereupon cease to be a Member of the Society.

28.—The Council shall draw up and submit for the approval of the Society, supplementary rules regulating the dates, places, and character of the meetings; shall propose special subjects for investigation by the Society, and shall nominate sub-committees for the methodical carrying out of such investigations. They shall decide, from time to time, on the form of publication which its proceedings are to assume.

29.—No alteration shall be made in the present rules, excepting at the Annual Meeting, or at a Special Meeting convened for the purpose, and unless it be proposed by the Council, or in writing by at least twenty Members, the usual notice be given of the proposed change to every Member before the meeting at which it is to be brought forward.

Each Member receives quarterly, from the beginning of the year in which he is elected, a copy of "BRAIN; a Journal of Neurology," the organ of the Society, and edited for it by A. de Watteville, M.A., M.D., B.Sc.

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*** Members are requested to communicate with the Secretaries when corrections are necessary.

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EXPLANATION OF ABBREVIATIONS.

O.M., Original Member.
Pres., President.
V.P., Vice-President.
Tr., Treasurer.
Sec., Secretary.
C., Member of Council.
H.J.L., Hughlings Jackson Lecturer.

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1892 Gotch, Francis, M.A., F.R.S., The Lawn, Banbury Road, Oxford.
1893 Grant, Dundas, M.D., F.R.C.S., 8, Upper Wimpole Street, W.
O.M. Gunn, R. Marcus, M.B., F.R.C.S., 54, Queen Anne Street, W. (C., 1899-1900.)
1895 Guthrie, Leonard, M.D., M.R.C.P., 15, Upper Berkeley Street, W.

1893 Halliburton, William Dobinson, M.D., F.R.C.P., F.R.S., Church Cottage, 17, Marylebone Road, N.W.
O.M. Hamilton, D. J., M.B., F.R.S.E., University, Aberdeen.
1898 Hanbury, William R., M.R.C.S., L.R.C.P., 27, Station Road, Watford.
1897 Harris, Wilfred J., M.D., M.R.C.P., 19, Oxford Terrace, W.
1898 Hartley, W. Darley, M.D., M.R.C.P., "Mayfield," Gilmore Hill Road, Cape Town, South Africa.
„ Haslett, John Hanfield, M.R.C.S., L.R.C.P., Halliford House, Sunbury-on-Thames.
1891 Hawkins, Herbert Pennell, M.D., F.R.C.P., 56, Portland Place, W.
O.M. Haycraft, J. B., M.B., F.R.S.E., The University, Cardiff.
1891 Head, Henry, M.D., M.R.C.P., F.R.S., 61, Wimpole Street, W. (C., 1900.)
O.M. Hill, Alex., M.A., M.D., Downing Lodge, Cambridge. (Pres., 1896; V.P., 1895; C., 1892-94.)

Elected

O.M. Hopkins, John, F.R.C.S., London Sick Asylum, Cleveland Street, W.

,, Horsley, Victor, F.R.C.S., F.R.S., 25, Cavendish Square, W. (Pres., 1898; V.P., 1896-97; C., 1892-93, 1899.)

1889 Huggard, William R., M.D., F.R.C.P., Davoz Platz, Switzerland.

1896 Hulme, George Frederick, M.D., C.M., Montague Road, Felixstowe.

1889 Humphry, Laurence, M.D., M.R.C.P., 3, Trinity Street, Cambridge.

O.M. Hutchinson, Jonathan, F.R.C.S., F.R.S., 15, Cavendish Square, W. (Pres., 1889; V.P., 1887-88; C., 1886. 1890.)

1889 Hyslop, T. B., M.D., C.M., Bethlem Royal Hospital, Lambeth, S.E.

O.M. Jackson, J. Hughlings, M.D., F.R.C.P., F.R.S., 3, Manchester Square, W. (Pres., 1886; H.J.L., 1897; C., 1887-92.)

,, Jessop, W. H., M.B., F.R.C.S., 73, Harley Street, W.

1895 Johnston, George, M.D., M.R.C.P., 3 Montagu Place, Montagu Square, W.

1892 Jones, Henry Lewis, M.D., F.R.C.P., 61, Wimpole Street, W.

1894 Jones, Robert, M.D., F.R.C.S., Claybury Asylum, Woodford, Essex.

,, Kidd, Percy, M.D., F.R.C.P., 60, Brook Street, W.

1896 Langdon, F. W., M.D., Cincinnati, Ohio, U.S.A.

1898 Langdon-Down, Reginald L., M.B., B.Ch., M.R.C.P., 81, Harley Street, W.

O.M. Langley, J. N., M.A., D.Sc., F.R.S., Trinity College, Cambridge. (C., 1898-99.)

1888 Lawford, J. B., M.D., F.R.C.S., 99, Harley Street, W.

O.M. Lees, D. B., M.D., F.R.C.P., 22, Weymouth Street, W. (C., 1900.)

1897 Lewis, H. Wolseley, M.R.C.S., L.R.C.P., Claybury Asylum, Woodford, Essex.

1899 Lord, John R., M.B., C.M., London County Asylum, Bexley, Kent.

1897 Lowenthal, Max, M.D., M.R.C.P., 126, Princes' Road, Liverpool.

1898 MacCormac, John M'Gee, M.D., L.R.C.P., L.R.C.S.Edin., 31, Victoria Place, Belfast.

,, McAldowie, Alexander M., M.D., 6, Brook Street, Stoke-on-Trent.

1891 Macdonald, Peter William, M.D., C.M., The County Asylum, Dorchester, Dorset.

,, Mackenzie, Hector William Gavin, M.D., F.R.C.P., 59, Welbeck Street, W.

O.M. Mackenzie, Stephen, M.D., F.R.C.P., 18, Cavendish Square, W. (C., 1896-98).

1896 Mackintosh, Ashley W., M.A., M.D., Wellington House, Alford Place, Aberdeen.

1899 MacLulich, Peers, M.D., B.Ch., Joint Counties Asylum, Carmarthen.

Elected
1889 Macphail, S. R., M.D. Borough Asylum, Rowditch, Derby.
O.M. Maguire, Robert, M.D., F.R.C.P., 4, Seymour Street, W. (Sec., 1890-93; C., 1893-95.)
,, Mann, J. Dixon, M.D., F.R.C.P., 16, St. John's Street, Manchester.
1894 Martin, Sidney, M.D., F.R.C.P., F.R.S., 10, Mansfield Street, W.
1891 May, W. Page, M.D., M.R.C.P., Helouan, Cairo, Egypt.
1890 Menzies, William Francis, M.D., B.Sc., M.R.C.P., Cheddleton Asylum, Leek, Staffordshire.
O.M. Mercier, C., M.B., M.R.C.P., Flower House, Southend, Catford, S.E. (C., 1899-1900.)
1897 Meyer, Adolf, M.D., Clark University, Worcester, Mass., U.S.A.
O.M. Mickle, W. Julius, M.D., F.R.C.P., Grove Hall Asylum, Bow, E. (V.P., 1900; C., 1895-97.)
1895 Moore, Norman, M.D., F.R.C.P., 94, Gloucester Place, W.
O.M. Morris, Malcolm, F.R.C.S.Ed., 8, Harley Street, W.
1888 Mott, F. W., M.D., F.R.C.P., F.R.S., 25, Nottingham Place, W. (Sec., 1894-98; C., 1899-1900.)
1899 Mould, Gilbert E., M.R.C.S., L.R.C.P., Dyffryn Aled, Abergele.
1894 Murray, George R., M.A., M.D., F.R.C.P., 11, Ellison Place, Newcastle-on-Tyne.
1889 Murray, H. Montague, M.D., F.R.C.P., 27, Saville Row, W.

O.M. Nettleship, Edward, F.R.C.S., 5, Wimpole Street, W.
,, Nicolson, David, C.B., M.D., M.R.C.P.Ed., Elmhyrst, Guildford, Surrey.
1888 Niermeyer, J. H. H., M.D., Amsterdam.
,, Norman, Conolly, F.R.C.P.I., F.R.C.S.I., St. Dymphna's, N. Circular Road, Dublin.

1887 Ogilvie, George, M.B., M.R.C.P., 22, Welbeck Street, W.
,, Ogilvie, Leslie, M.B., M.R.C.P., 46, Welbeck Street, W.
,, Oliver, Thomas, M.D. F.R.C.P., 7, Ellison Place, Newcastle-on-Tyne.
O.M. Orange, Wm., C.B., M.D., F.R.C.P., The Bryn, Godalming, Surrey.
,, Ord, W. M., M.D., F.R.C.P., 37, Upper Brook Street, W. (C., 1893-94.)
,, Ormerod, J. A., M.D., F.R.C.P., 25, Upper Wimpole Street, W. (C., 1895-97.)
,, Orr, David, M.B., County Asylum, Prestwich, Manchester.

,, Page, Herbert William, M.A., F.R.C.S., 146, Harley Street, W. (V.P., 1900, C., 1891-92.)
1895 Parkinson, John Porter, M.D.Lond., M.R.C.P., 57, Wimpole Street, W.
1896 Paterson, Donald Rose, M.D., M.R.C.P., 18, Windsor Place, Cardiff.
1895 Pinder, George, M.D., B.C., Hazeldene, Farncombe Road, Worthing.
1899 Piper, Francis P., M.B., M.R.C.S., L.R.C.P., Claybury Asylum, Woodford, Essex.

Elected

1888 Pitt, G. N., M.D., F.R.C.P., 15, Portland Place, W.

O.M. Poore, G. Vivian, M.D., F.R.C.P., 32, Wimpole Street, W. (C. 1898-99.)

,, Purves, W. Laidlaw, M.D., 20, Stratford Place, W.

1899 Rambaut, Daniel F., M.D., B.Ch., Richmond District Asylum, Dublin.

1894 Ransom, William B., M.D., F.R.C.P., The Pavement, Nottingham.

1890 Rayner, Henry, M.D., M.R.C.P.Ed., 16, Queen Anne Street, W.

O.M. Reid, E. W., M.B., F.R.S., University College, Dundee.

1897 Reissmann, Charles H., B.A., B.Sc., Saxony Villas, Oppidans Road, Primrose Hill.

1893 Rennie, George E., M.D., M.R.C.P., College Street, Sidney.

1895 Reynolds, Ernest S., M.D., F.R.C.P., 23, St. John Street, Manchester.

1892 Richards, Joseph Peeke, M.R.C.S., 6, Freeland Road, Ealing, W.

1891 Rivers, W. H. R., M.A., M.D., F.R.C.P., St. John's College, Cambridge. (C., 1897-98.)

1898 Robertson, William Ford, M.D., 12, Brisco Place, Edinburgh.

1892 Rowe, Edmund Lewis, L.R.C.P., L.R.C.S., Borough Asylum, Ipswich.

,, Ruffer, Marc Armand, M.D., Cairo.

1889 Russell, J. S. Risien, M.D., F.R.C.P., 4, Queen Anne Street, W. (Sec., 1896-1900.)

1899 Russell, J. W., M.D., M.R.C.P., 72, Newhall Street, Birmingham.

O.M. Sanderson, Sir J. Burdon, M.D., F.R.C.P., F.R.S., Banbury Road, Oxford.

,, Savage, G. H., M.D., F.R.C.P., 3, Henrietta Street, Cavendish Square. (Pres., 1897; V.P., 1895; C., 1886-90, 1898.)

1888 Savill, T. D., M.D., M.R.C.P., 60, Upper Berkeley Street, W.

O.M. Schäfer, E. A., F.R.S., University of Edinburgh. (Pres., 1893; V.P., 1892; C. 1886-90.)

,, Semon, Sir Felix, M.D., F.R.C.P., 39, Wimpole Street, W. (C., 1890-1900.)

1898 Seward, Wm. Joseph, M.B., Colney Hatch Asylum, N.

O.M. Sharkey, S. J., M.D., F.R.C.P., 22, Harley Street, W. (C., 1889-92.)

,, Sherrington, C. S., M.D., F.R.S., 16, Grove Park, Liverpool. (C. 1892-95.)

1894 Shuttleworth, George E., M.D., Ancaster House, Richmond.

1898 Simpson, Francis O., L.R.C.P., M.R.C.S., Rainhill Asylum, Liverpool.

1895 Smith, F. J., M.D., M.R.C.P., 138, Harley Street, W.

1887 Smith, R. Percy, M.D., F.R.C.P., 36, Queen Anne Street, W.

1895 Smith, Telford, M.D., B.S., 54, South Hill Park, Bromley, Kent.

,, Spicer, W. T. Holmes, M.D., F.R.C.S., 47 Welbeck Street, W.

,, Stansfield, Thos. E. K., M.B., London County Asylum, Bexley, Kent.

Elected

1895 STANLEY, DOUGLAS, M.D., 9, Easy Row, Birmingham.

1892 STARLING, ERNEST HENRY M.D., F.R.C.P., F.R.S., 8, Park Square, N.W.

1897 STEWART, PURVES, M.A., M.D., M.R.C.P., 133, Harley Street, W.

„ STIRLING, WM., M.D., D.Sc., Owens College, Manchester.

1897 STODDART, WM. H., M.D., B.S., M.R.C.P., Bethlem Royal Hospital, Lambeth, S.E.

1895 STOUT, G. F., M.A., St. John's College, Cambridge.

1887 SUCKLING, C. W., M.D., M.R.C.P., 103, Newhall Street, Birmingham.

1889 SUTHERLAND, HENRY, M.D., M.R.C.P., 21, New Cavendish Street, Portland Place, W.

1888 SYERS, HENRY W., M.D., M.R.C.P., 75, Wimpole Street, W.

1898 TAYLOR, F. R. P., M.D., B.S., Darenth Asylums and Schools, Dartford, Kent.

1891 TAYLOR, JAMES, M.D., F.R.C.P., 49, Welbeck Street, W. (C. 1900.)

1898 THOMSON, H. CAMPBELL, M.D., M.R.C.P., 34, Queen Anne Street, W.

1889 THORBURN, WM., F.R.C.S., The Limes, Nelson Street, Manchester.

1892 TITCHENER, E. B., B.A., Ph.D., 72, Heustis Street, Ithaca, N.Y.

O.M. TOOTH, H. H., M.D., F.R.C.P., 34, Harley Street, W. (Sec., 1891-95; C., 1896-99.)

1892 TREVELYAN, E. F., M.D., B.Sc., M.R.C.P., 40, Park Square, Leeds.

1892 TUCKEY, CHARLES LLOYD, M.D., C.M., 88, Park Street, Grosvenor Square, W.

1892 TUKE, Sir J. BATTY, M.D., F.R.C.P.Ed., 20, Charlotte Sq., Edinburgh.

1891 TUKE, THOMAS SEYMOUR, M.B., M.R.C.S., Chiswick House, Chiswick.

„ TURNER, WILLIAM ALDREN, M.D., F.R.C.P., 13, Queen Anne Street, W.

1898 TURNEY, HORACE G., M.D., M.Ch., F.R.C.P., 68, Portland Place, W.

O.M. TWEEDY, JOHN, F.R.C.S., 100, Harley Street, W.

1888 VOORTHUS, J. A., M.D., Apeldoorn, 542, Loulaan, Netherlands.

1895 WADE, ARTHUR L., M.D., Somerset and Bath Asylum, Wells.

1894 WALKER, A. STODART, M.B., 30, Walker Street, Edinburgh.

O.M. WALLER, AUGUSTUS, M.D., F.R.S., 16, Grove End Road, N.W. (Pres., 1900; V.P., 1899; C., 1894-97.)

„ WARD, J., D.Sc., Trinity College, Cambridge.

[illegible] WARNER, FRANCIS, M.D., F.R.C.P., 5, Prince of Wales Terrace, Kensington Palace, W.

1892 WASHBOURN, J. W., M.D., F.R.C.P., 6, Cavendish Place, W.

O.M. WATTEVILLE, A. DE, M.A., M.D., B.Sc., 30, Welbeck Street, W. (C., 1890-95, 1896-1900; Sec., 1886-89; Editor of *Brain*.)

1897 WEBER, F. PARKES, M.D., F.R.C.P., 19, Harley Street, W.

„ WEST, SAMUEL, M.D., F.R.C.P., 15, Wimpole Street, W.

Elected	
1897	WHITE, ERNEST W., M.B., M.R.C.P., City of London Asylum, Dartford.
O.M.	WHITE, W. HALE, M.D., F.R.C.P., 65, Harley Street, W. (C., 1897-1900).
1894	WHITING, ARTHUR J., M.D., M.R.C.P., 142, Harley Street, W.
1889	WIGLESWORTH, JOSEPH, M.D., F.R.C.P., County Asylum, Rainhill, Lancashire.
1894	WILLIAMSON, RICHARD T., M.D., M.R.C.P., 294, Oxford Road, Manchester.
1896	WILSON, ALBERT, M.D., M.R.C.P., 33, Fairlop Road, Leytonstone.
,,	WOOD, GUY M., M.B., M.R.C.P., 9, Endsleigh Street, W.C.
1889	WOOD, T. OUTTERSON, M.D., M.R.C.P., 10, Margaret Street, Cavendish Square, W.
1892	WOODHEAD, G. SIMS, M.D., F.R.C.P.Ed., Pathological Laboratory, Cambridge.
1899	WRIGHT, HAMILTON, M.D., Claybury Hall, Woodford Bridge, Essex.
1898	YOUNG, ROBERT ARTHUR, M.D., B.Sc., M.R.C.P., 41, Wimpole St., W.